

**Pharmaceuticals: Merck**  
**Sustaining Long-term Advantage**  
**Through Information Technology**

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## **PHARMACEUTICALS: MERCK**

**Sustaining Long-term Advantage Through Information Technology**

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## **Table of Contents**

- 1. Introduction: Objective of this Study**
- 2. The Pharmaceutical Industry in a Global Context**
- 3. Product R&D and Clinical Trials**
- 4. Manufacturing and Process R&D**
- 5. Technological Factors**
  - Structure-Based Drug (“Rational Drug”) Design**
  - Structure-Based Drug (“Rational Drug”) Design**
- 6. Merck**
- 7. Managerial Decision Making**
- 8. Decision Making on IT projects**
- 9. Joint Ventures**
- 10. Information Technology and Organization**
- 11. Appendix I - Summary Answers to Questions for Merck - Strategy & Operations**
- 12. Appendix II - INDUSTRY AND FIRM BUSINESS DATA**
- 13. Bibliography**

## Introduction: Objective of this Study

This case study of Merck was completed under a three year research grant from the Sloan Foundation. The project's purpose is to examine in a series of case studies how U.S. and Japanese firms who are recognized leaders in using information technology to achieve long-term sustainable advantage have organized and managed this process. While each case is complete in itself, each is part of this larger study.<sup>1</sup>

This pharmaceutical industry case together with other cases<sup>2</sup> support an initial research hypothesis that leading software users in both the U.S. and Japan are very sophisticated in the ways they have integrated software into their management strategies and use it to institutionalize organizational strengths and capture tacit knowledge on an iterative basis. In Japan this strategy has involved heavy reliance on customized and semi-customized software (Rapp 1995) but is changing towards a more selective use of package software managed via customized systems. In turn, U.S. counterparts, such as Merck, who have often relied more on packaged software, are doing more customization, especially for systems needed to integrate software packages into something more closely linked with their business strategies, markets, and organizational structure. Thus, coming from different directions, there appears some convergence in approach by these leading software users. The cases thus confirm what some other analysts have hypothesized, a coherent business strategy is a necessary condition for a successful information technology strategy (Wold and Shriver 1993).<sup>3</sup> These strategic links for Merck are presented in the following case.

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<sup>1</sup> Industries and firms examined are food retailing (Ito-Yokado and H. Butts), semiconductors (NEC and AMD), pharmaceuticals (Takeda and Merck), retail banking (Sanwa and Citibank), investment banking (Nomura and Credit Suisse First Boston), life insurance (Meiji and USAA), autos (Toyota), steel (mini-mills and integrated mills, Nippon Steel, Tokyo Steel and Nucor), and apparel retailing (WalMart). The case writer and the research team wish to express their appreciation to the Alfred P. Sloan Foundation for making this work possible and to the Sloan industry centers for their invaluable assistance. They especially appreciate the time and guidance given by the center for research on pharmaceuticals at MIT as well as Mr. Sato at Takeda.

<sup>2</sup> This refers to cases for which interviews have been completed. See footnote 3.

<sup>3</sup> These and other summary results are presented in another Center on Japanese Economy and Business working paper: William V. Rapp, "Gaining and Sustaining Long-term Advantage Through Information Technology: The Emergence of Controlled Production," December 1998

strategy (Wold and Shriver 1993).<sup>3</sup> These strategic links for Merck are presented in the following case.

Yet this case along with the other cases also illustrates that implementation and design of each company's software and software strategy is unique to its competitive situation, industry and strategic objectives. These factors influence how they choose between packaged and customized software options for achieving specific goals and how they measure their success. Indeed, as part of their strategic integration, Merck and the other leading software users interviewed have linked their software strategies with their overall management goals through clear mission statements that explicitly note the importance of information technology to firm success.

They have coupled this with active CIO (Chief Information Officer) and IT (information technology) support group participation in the firm's business and decision making structure. Thus for firms like Merck the totally independent MIS (Management Information Systems) department is a thing of the past. This may be one reason why outsourcing for them has not been a real option, though their successful business performance is not based solely on software. Rather as shall be described below software is an integral element of their overall management strategy and plays a key role in serving corporate goals such as enhancing productivity, improving inventory management or strengthening customer relations. These systems thus must be coupled with an appropriate approach to manufacturing, R&D, and marketing reflecting Merck's clear understanding of their business, their industry and their firm's competitive strengths within this context. This clear business vision has enabled them to select, develop and use the software they require for each business function and to integrate these into a total support system for their operations to achieve corporate objectives. Since this vision impacts other corporate

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<sup>3</sup> These and other summary results are presented in another Center on Japanese Economy and Business working paper: William V. Rapp, "Gaining and Sustaining Long-term Advantage Through Information Technology: The Emergence of Controlled Production," December 1998

decisions, they have good human resource and financial characteristics too (Appendix I & II).

Yet Merck does share some common themes with other leading software users such as the creation of large proprietary interactive databases that promote automatic feedback between various stages and/or players in the production, delivery and consumption process. Their ability to use IT to reduce inventories and improve control of the production process are also common to other leading software users. They are also able organizationally and competitively to build beneficial feedback cycles or loops that increase productivity in areas as different as R&D, design and manufacturing while reducing cycle times and defects or integrating production and delivery. Improved cycle times reduce costs but increase the reliability of forecasts since they need to cover a shorter period. Customer satisfaction and lower inventories are improved through on-time delivery. Thus, software inputs are critical factors in Merck's and other leading users' overall business strategies with strong positive competitive implications for doing it successfully and potentially negative implications for competitors.

An important consideration in this respect is the possible emergence of a new strategic manufacturing paradigm in which Merck is probably a leading participant. In the same way mass production dramatically improved on craft production through the economies of large scale plants that produced and used standardized parts and lean production improved on mass production through making the production line more continuous, reducing inventories and tying production more closely to actual demand, what might be called "controlled" production seems to significantly improve productivity through monitoring, controlling and linking every aspect of producing and delivering a product or service including after sales service and repair.

Such controlled production is only possible by actively using information technology and software systems to continuously provide the monitoring and control function to what had previously been a rather automatic system response to changes in

expected or actual consumer demand. This may be why their skillful use of information technology is seen by themselves and industry analysts as important to their business success, but only when it is integrated with the business from both an operation and organization standpoint reflecting their overall business strategy and clarity of competitive vision. Therefore at Merck the software and systems development people are part of the decision making structure while the system itself is an integral part of organizing, delivering and supporting its drug pipeline from R&D through to sales post FDA approval. This sequence is particularly critical in pharmaceuticals where even after clinical trials there is a continuous need to monitor potential side effects.

Therefore Seagate Technology may be correct for Merck too when they state in their 1997 Annual Report **“We are experiencing a new industrial revolution, one more powerful than any before it. In this emerging digital world of the Third Millennium, the new currency will be information. How we harness it will mean the difference between success and failure, between having competitive advantage and being an also-ran.”**

In Merck’s case, as with the other leading software users examined, the key to using software successfully is to develop a mix of packaged and customized software that supports their business strategies and differentiates them from competitors. However, they have not tried to adapt their organizational structure to the software. Given this perspective, functional and market gains have justified the additional expense incurred through customization, including the related costs of integrating customized and packaged software into a single information system. They do this by assessing the possible business uses of software organizationally and operationally and especially its role in enhancing their core competencies. While they will use systems used by competitors if there is no business advantage to developing their own, they reject the view that information systems

are generic products best developed by outside vendors who can achieve low cost through economies of scale and who can more easily afford to invest in the latest technologies.<sup>4</sup>

In undertaking this and the other case studies, the project team sought to answer certain key questions while still recognizing firm, country and industry differences. These have been explained in the summary paper referenced in footnote 3. We have set them forth in Appendix I where Merck's profile is presented based on our interviews and other research. Readers who wish to assess for themselves the way Merck's strategies and approaches to using information technology address these issues may wish to review Appendix I prior to reading the case. For others it may be a useful summary.<sup>5</sup>

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<sup>4</sup> Merck and the other cases have been developed using a common methodology that examines cross national pairs of firms in key industries. In principle, each pair of case studies focuses on a Japanese and American firm in an industry where software is a significant and successful input into competitive performance. The firms examined are ones recognized by the Sloan industry centers and by the industry as ones using software successfully<sup>4</sup>. To develop the studies, we combined analysis of existing research results with questionnaires and direct interviews. Further, to relate these materials to previous work as well as the expertise located in each industry center, we held working meetings with each center and coupled new questionnaires with the materials used in the previous study to either update or obtain a questionnaire similar to the one used in the 1993-95 research (Rapp 1995). This method enabled us to relate each candidate and industry to earlier results. We also worked with the industry centers to develop a set of questions that specifically relate to a firm's business strategy and software's role within that. Some questions address issues that appear relatively general across industries such as inventory control. Others such as managing the drug pipeline are more specific to a particular industry. The focus has been to establish the firm's perception of its industry and its competitive position as well as its advantage in developing and using a software strategy. The team also contacted customers, competitors, and industry analysts to determine whether competitive benefits or impacts perceived by the firm were recognized outside the organization. These sources provided additional data on measures of competitiveness as well as industry strategies and structure. The case studies are thus based on extensive interviews by the project team on software's use and integration into management strategies to improve competitiveness in specific industries, augmenting existing data on industry dynamics, firm organizational structure and management strategy collected from the Sloan industry enters. In addition, we gathered data from outside sources and firms or organizations with which we worked in the earlier project. Finally, the US and Japanese companies in each industry that were selected on the basis of being perceived as successfully using software in a key role in their competitive strategies in fact saw their use of software in this exact manner while these competitive benefits were generally confirmed after further research.

<sup>5</sup> The questions are broken into the following categories: General Management and Corporate Strategy, Industry Related Issues, Competition, Country Related Issues, IT Strategy, IT Operations, Human Resources and Organization, Various Metrics such as Inventory Control, Cycle Times and Cost Reduction, and finally some Conclusions and Results. They cover a range of issues from direct use of software to achieve competitive advantage, to corporate strategy, to criteria for selecting software, to industry economics, to measures of success, to organizational integration, to beneficial loops, to training and institutional dynamics, and finally to interindustry comparisons.



## **The Pharmaceutical Industry in a Global Context**

In advanced countries that represent Merck's primary market, the pharmaceutical industry is an exceptionally research intensive industry where many firms are large multinationals (MNCs). It is also heavily regulated for both local producers and MNCs. Regulations work as both constraints and performance boosters since drugs are used with other medical and healthcare services. Therefore, healthcare expenditures are divided among many industries and providers of which pharmaceuticals are only one. All parties involved are interested in influencing the regulatory environment and in participating in the growth in healthcare services. This means understanding the industry requires appreciating its political economic context. In this regard, healthcare providers in rich nations are currently under pressure to control costs due to aging populations. Regulators who have the authority to change the demand structure through laws and regulations are considering various measures to reduce costs such as generic drug substitution which may mean lower returns for discovering and developing drugs. Still, if drugs are more effective at reducing healthcare costs compared to other treatments, Pharmaceutical companies can benefit. Since R&D is at the heart of competition, each drug company must respond to these cost containment pressures cautiously and strategically in competing for healthcare expenditures.

Another important aspect of this industry is technological change arising from the convergence of life and biological sciences. Many disciplines now work together to uncover the mechanisms that lie behind our bodies and various diseases. Examples are molecular biology, cell biology, biophysics, genetics, evolutionary biology, and bioinformatics. As scientists see life from these new chemical and physical viewpoints, the ability to represent, process and organize the massive data based on these theories becomes critical. Because computers are very flexible scientific instruments (Rosenberg 1994), progress in information technology and computer science has broadened scientific frontiers for the life and biological sciences. These advances have opened new doors to

attack more complex diseases, including some chronic diseases of old age. These therapeutic areas are present opportunities for pharmaceutical companies since they address demographic and technical changes in advanced countries. Still, to take advantage of these opportunities requires information technology capabilities.

Historically, the drug industry has been relatively stable where the big players have remained unchanged for years. This has been due to various entry barriers such as R&D costs, advertising expense, and strong expertise in managing clinical trials. It is difficult and expensive for a new company to acquire this combination of skills quickly. However, there are signs the industry and required mix of skills may be changing. There have been several cross national mergers especially between U.S. and European companies. In addition, new biotechnology companies are very good at basic research, which may force pharmaceutical R&D to transform itself. For example, no single company even among the new mega-companies is large enough to cover all new areas of expertise and therapeutic initiatives. Thus, many competitors have had to form strategic alliances to learn or access new technologies and to capture new markets. Conversely, a stand-alone company can have a lot to lose. The challenge facing large pharmaceutical companies is how fast and how effectively they can move to foster both technological innovation and cost containment without exposing themselves to too much risk.

The pharmaceutical industry in all of Merck's major markets reflects these cost containment pressures, the need to harmonize expensive and time consuming clinical trials, and the impact of extensive regulations. Information technology has had its impacts too. For example, to respond to these challenges Merck is using more management techniques based on consensus decision making among top functional managers. This requires better communication support using e-mail and groupware combined with face-to-face communication. This is part of an industry trend towards greater parallel decision making in R&D and less sequential decision making where A must first concur on a project before moving to B, etc. Now all elements of the firm evaluate the project simultaneously at each

stage. In this manner, Merck has significantly reduced coordination costs while centralizing and speeding the overall decision making process. Additionally, first-tier firms have had to follow a trend in R&D strategies that increasingly use information technologies. Exchange of data and ideas across national borders has become relatively easy, and contracts may specify access to another company's database. Because many companies share similar R&D instruments and methods, one company's instruments may be compatible with other companies'. Indeed, the trend towards greater use of Web-based technology in R&D and other operations may change our notion of a firm and its boundaries. Firms may eventually be characterized by knowledge creating capabilities (Nonaka and Takeuchi 1995). Having more ways to communicate with other companies makes frequent communication with greater nuance possible. This supports the trend towards more strategic alliances unless overtaken by the creation of larger firms through continued mergers.

This is also partially due to the nature of the industry which is part of the fine chemical industry where changes in technologies are rapid and often discontinuous. It therefore requires different management skills from other technology based industries, especially as the knowledge required for innovation tends to be more specialized thus demanding less coordination than assembly industries. Transferring mass production know-how to R&D is also limited. Still, the U.S. and European industries have been undergoing massive reorganization to achieve economies of scope and scale in R&D and marketing where firms are taking advantage of the fact that the U.S. industry is much less regulated than most foreign industries (Bogner and Thomas 1996).

The U.S. companies grew after World War II due to a huge home market combined with the global market for antibiotics this was before British firms began to recapture market share. At that time, European firms did not have the resources to sell drugs directly to U.S. doctors. The European recovery period gave U.S. firms enough time to take advantage of antibiotics. Then, when the U.S. market became saturated, U.S.

firms expanded into global markets in the early 1960s. This forced U.S. firms to diversify their R&D as well. At the same time, in 1962 amendments to the Food, Drug and Cosmetic Act increased the rigor of drug regulation creating an entry barrier to industry R&D that favored large established firms (Bogner and Thomas 1996). The U.S. effectively tightened their regulations after their industry had acquired sufficient R&D skills and resources. This timing seems to account for today's industry success. Another factor is that unlike the European industry, U.S. firms had few incentives to integrate vertically. During the War the military distributed antibiotics. Therefore, the U.S. firms were generally bulk chemical producers such as Merck and Pfizer or sellers of branded drugs such as Abbott and Upjohn. At the end of the War, only a few firms such as Squibb were fully integrated. However, as promotion and other downstream functions became more critical, controlling functions such as distribution became a strategic objective. To accomplish this they acquired other firms (Merck acquired Sharpe and Dohme and Pfizer acquired Roerig), developing expansion via merger and acquisition as a business strategy and core competency. This helped lay the foundation for subsequent industry consolidation.

Today, American healthcare is based on the belief that while making progress in science is the best way to solve medical problems, cost containment is also important. As a result, while American healthcare is the most expensive in the world, it is also not available to everyone and is the most subject to cost scrutiny. Indeed, since drugs are just one way to improve health, consumers should want to remain healthy and choose cost effective means to do this. However, the reality is that insurance systems covering different services give incentives and disincentives for particular care (Schweitzer 1997). Thus, coordinated adjustment of prices for healthcare is necessary to get markets for healthcare products to work better. In the U.S., this has led to a public policy push for HMOs. These healthcare purchasers have in turn set the reward schemes available to healthcare providers such as pharmaceutical companies so as to reduce transaction costs (Ikegami and Campbell 1996)

and promote innovation. These developments and trends are putting more pressure on major firms to put more resources into R&D, to focus more critically on just ethical drug development for the global market, and to be more careful in gathering information on clinical trials and side effects.

The most important market for Merck in this regard is the U.S. where NIH has pursued a unified approach. This is because the NIH (The National Institutes of Health) has actively supported basic life science research in U.S. universities, especially after World War II. NSF (National Science Foundation) also encouraged collaboration between academia and industry with partial funding by the government. Other federal and state funding has been important to the scientific community as well, especially in biotechnology. In biotechnology, the funding of basic research has led to a complex pattern of university-industry interaction that includes gene patenting and the immediate publishing of results (Rabinow 1996). U.S. drug companies are of course profit motivated but are regulated by the FDA (Federal Drug Administration) which is rigorous about its drug approvals, demanding clear scientific evidence in clinical research as its operation is basically science oriented.

### **Product R&D and Clinical Trials**

Still, despite this R&D support, industry economics are driven by pharmaceutical R&D's very lengthy process, composed of discovering, developing and bringing to market new ethical drugs with the latter heavily determined by the drug approval process in major markets such as the U.S., Europe and Japan<sup>6</sup>. These new therapeutic ethical products fall into four broad categories (U.S. Congress, OTA 1993): one, new chemical entities (NCEs) - new therapeutic entities (NTEs) - new therapeutic molecular compounds never before used or tested in humans; two, drug delivery mechanisms - new approaches to delivering therapeutic agents at the desired dose to the desired part of the body; three,

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<sup>6</sup> Ethical drugs are biological and medicinal chemicals advertised and promoted primarily to the medical, pharmacy, and allied professions. Ethical drugs include products available only by prescription as well as some over-the-counter drugs (Pharmaceutical Manufacturers Association 1970-1991).

next stage products - new combinations, formulations, dosing forms, or dosing strengths of existing compounds that must be tested in humans before market introduction; four, generic products - copies of drugs not protected by patents or other exclusive marketing rights.

From the viewpoint of major pharmaceutical firms such as Merck, NCEs are the most important for the R&D of innovative drugs that drive industry success. Since it is a risky and very expensive process, understanding a company's R&D and drug approval process is critical to understanding the firm's strategy and competitiveness both domestically and globally. Statistics indicate that only about 1 in 60,000 compounds synthesized by laboratories can be regarded as "highly successful" (U.S. Congress, OTA 1993). Thus, it is very important to stop the R&D process whenever one recognizes success is not likely. Chemists and biologists used to decide which drugs to pursue, but R&D is now more systematic and is a collective company decision since it can involve expenditures of \$250 to \$350 million prior to market launch, thus the need for more parallel decision making. Key factors in the decision making process are expected costs and returns, the behavior of competitors, liability concerns, and possible future government policy changes (Schweitzer 1997). Therefore, stage reviews during drug R&D are common, and past experiences in development, manufacturing, regulatory approvals, and marketing can provide ample guidance.

NCE's are discovered either through screening existing compounds or designing new molecules. Once synthesized, they go through a rigorous testing process. Their pharmacological activity, therapeutic promise, and toxicity are tested using isolated cell cultures and animals as well as computer models. It is then modified to a related compound to optimize its pharmacological activity with fewer undesirable biological properties (U.S. Congress, OTA 1993). Once preclinical studies are completed and the NCE has been proven safe on animals, the drug sponsor applies for Investigational New Drug (IND) status. If it receives approval, it starts Phase I clinical trials to establish the

tolerance of healthy human subjects at different doses to study pharmacological effects on humans in anticipated dosage levels. It also studies its absorption, distribution, metabolism, and excretion patterns. This stage requires careful supervision since one does not know if the drug is safe on humans.

During phase II clinical trials a relatively small number of patients participate in controlled trials of the compound's potential usefulness and short term risks. Phase III trials gather precise information on the drug's effectiveness for specific indications, determine whether it produces a broader range of adverse effects than those exhibited in the smaller phase I and II trials. Phase III trials can involve several hundred to several thousand subjects and are extremely expensive. Stage reviews occur before and during each phase, and drug development may be terminated at any point in the pipeline if the risk of failure and the added cost needed to prove effectiveness outweigh the weighted probability of success.

There is a data and safety monitoring board in the U.S.. This group has access to "unblinded data" throughout the conduct of a trial but does not let anyone else know what the data shows until it is necessary. For example, they will not divulge the efficacy data until the trial reaches a point where it seems appropriate to recommend stopping it because the null hypothesis of efficacy has been accepted or rejected. The FDA will usually insist on the drug proving efficacy with respect to ameliorating a disease before giving approval.

If clinical trials are successful, the sponsor seeks FDA marketing approval by submitting a New Drug Application (NDA). If approved, the drug can be marketed immediately, though the FDA often requires some amendments before marketing can proceed (Schweitzer 1997). However, successful drug development and sales not only requires approval of therapeutic value and validity but also that the manufacturing process meet stringent "best-practice" standards. To meet U.S. regulations, Phase IV trials are required. Manufacturers selling drugs must notify the FDA periodically about the

performance of their products. This surveillance is designed to detect uncommon, yet serious, adverse reactions typically not revealed during premarket testing. This postapproval process is especially important when phase III trials were completed under smaller fast track reviews. These additional studies usually include use by children or by those using multiple drugs where potential interactions can be important (Schweitzer 1997). Furthermore, because drug development costs are so high relative to production costs, patent protection is another key aspect of a company's management strategy. Under U.S. law, one must apply for a patent within one year of developing an NCE or the innovation enters the public domain. Therefore, patenting is usually early in the development cycle or prior to filing the NCE. But as this begins the patent life, shortening the approval period extends a drug's effective revenue life under patent. This makes managing clinical trials and the approval process an important strategic variable.

Although creating a drug pipeline through various stages of development is relatively standardized, it is changing as companies use different methods to reduce time and related costs of new drug development. Companies are constantly pressuring the authorities to reduce NDA review times. As a consequence, the FDA did introduce an accelerated approval process for new drugs in oncology, HIV (AIDS) and other life threatening illnesses. A familiar feature of this new fast track review is the use of surrogate end points, or proxies for clinical end points which are measured by laboratory values but lack supporting clinical outcomes data.

Accelerated approval speeds new drugs to market saving companies tens of millions of dollars in negative cash flow. However, it does not generate clinical values that insurers and managed care organizations demand. Countering this situation is thus the trend among drug firms to increase the complexity of their analyses during clinical trials. Companies have begun to use cost-effective analysis in their evaluation of new drugs in assessing competing product development investment alternatives and by integrating cost effectiveness analysis into their clinical trials. They also try to capture quality of life



measures such as how patients perceive their lives while using the new drug. Companies vary their analysis by country (Rettig 1997) since measures of effectiveness shift according to clinical practice, accessibility to doctors, and what different cultures value as important.

There are no universal measures of the quality of life. At present, the components measured depend largely on the objectives of each researcher but some companies are trying to introduce more systematic measures. Nevertheless, no matter what components are chosen for these studies, capturing, storing and using the data requires sophisticated software and data base management techniques which must be correlated with various families of molecules. Also, to avoid the moral hazard of focusing on the weaknesses in a competitor's drug or molecule, some analysts argue companies should examine all domains and their components (Spilker 1996) and move towards agreed performance standards. Furthermore, quality of life measures should only be used when they are of practical use to doctors in treating patients (Levine 1996). Such judgments should be sensitive and informed and should cover criteria related and important to a broad spectrum of patients while balancing measures which can be easily gathered and those that are more complex due to multiple treatments. These trends make clinical trials and data gathering complex and expensive and put a premium on a firm's ability to manage the process efficiently, including creating and using large patient and treatment databases.

### **Manufacturing and Process R&D**

The research process differs from production. Yet, both are important, particularly the firm's knowledge of scale-up. This is difficult because production requires uniformity at every stage. Making the average chemical make-up constant is not enough. Careful scale-up is essential to avoid contamination. Variations from the mean in commercial production must be very small. This requires constant control of variables such as the preparation of raw materials, solvents, reaction conditions, and yields. Often, experience will help achieve purer output in the intermediate processes. This better output alleviates problems in later processes. Thus, there is a learning curve in process R&D which starts at

the laboratory. An important distinction is between continuous process and batch process. In the continuous process, raw materials and sub-raw materials go into a flow process that produces output continuously. This continuous process is more difficult because many parameters and conditions have to be kept constant. This requires a good understanding of both optimizing the chemical process and maintaining safeguards against abnormal conditions. However, continuous processes are less dangerous and require fewer people to control at the site than batch processing where the chemicals are produced in batches, put in pill form and then stored for future distribution and sale (Takeda 1992).

The following compares initial process R&D once a compound is discovered and commercial manufacturing for a representative chemical entity proceeds (Pisano 1996).

Comparison research process and commercial production for representative chemical entity (Pisano 1996)

	Initial discovery process	Final commercial production process
Number of chemical steps	25	7
Equipment	Test Tubes □ 1-l flasks	2000-4000 gallon stainless steel vessels
Batch size (output) Operators	Approximately 1g Ph.D. chemists	100-200 kg Technicians □ Semi-skilled plant workers
Purity	1-10%	99%
Cost (kg <sup>-1</sup> )	Approximately \$20000-\$50000	Approximately \$3500
Criteria for process design	Biological activity of molecule □ □ patent issues	Cost Quality (purity) Conformance to drug and environment protection regulations Operability

Process R&D in chemical pharmaceuticals involves three stages: (1) process research, where basic process chemistry (synthetic route) is explored and chosen; (2) pilot development, where the process is run and refined in an intermediate-scale pilot plant; and (3) technology transfer and startup, where process is run at a commercial manufacturing site (Pisano 1997). Pisano argues that the scientific base of chemistry is more mature than biotechnology and this difference accounts for the more extensive use of computer simulations in drugs made by chemical synthesis than biotechnology-based drugs.

Codifying the knowledge in chemistry and chemical engineering in software has a higher explanatory power than in biotechnology. In chemistry, many scientific laws are available for process variables such as pressure, volume, and temperature. Computer models can simulate these in response to given parameters to predict cost, throughput and yield (Pisano 1997). By contrast, biotechnology has aspects that resemble art dependent on an operator's skill more than science which only requires the proper formulation. This is particularly true for large-scale biotechnology process (Pisano 1997). Simulation is thus less reliably extrapolated to commercial production. An additional factor is the importance of purification after large-scale production in bioreactors in biotechnology-based drugs. It is not rare at this stage of extraction and purification that commercial application becomes impossible, even though the scale-up is successful. Since avoiding contamination is the key in biotechnology-based drugs, extracting and purifying a small amount of the desired materials from a large amount of broth is critical. This process is done using filters, chromatography, and other methods specific to organisms (Koide 1994).

### **Technological Factors**

All scientific frontiers affect pharmaceutical companies. Since no company can be an expert on everything, what technology to develop in-house and what to license or subcontract have become important issues. In general, pharmaceutical companies were skeptical of new developments in small biotechnology firms. Yet the latter now provide new techniques in basic research and fermentation to the MNCs. Other pharmaceutical

companies then tend to follow when competitors adopt ideas from less well known biotech companies. This is why many such companies announce platform deals with drug companies to get more financial resources and opportunities. Biotechnology based pharmaceuticals have entered a new development stage which requires the capital, manufacturing and marketing expertise of the large companies.

New drug discovery methods and biotechnology each demand skills different from earlier times. Emerging biotech companies offer new ideas and research tools. Other new technologies such as stripping out side effects, specialized drug delivery systems, and “antisense” which cancels out the disease causing messages of faulty RNA also come from biotechnology (Fortune 1997). These are promising areas of drug research and potential products. Further, these biotech companies develop new drugs more quickly than large firms. Where they often have difficulty is in managing clinical trials and the approval process, an area where large firms have considerable experience and expertise, including sophisticated software for tracking the large data bases and handling the new computerized application procedure. In addition, biotechnology demands skills in large scale commercial production which smaller startups may not possess. Thus, close association with large firms is logical and efficient, and one should expect more future alliances and joint ventures, though outsourcing to organizations that will manage clinical trials is growing.

Another important factor which further encourages specialization in a network of companies is the industry’s heavy use of information technology. Indeed, software strategies have become an important part of the industry through their impact on R&D, drug approval, including clinical trials, and control of manufacturing. If decisions in a science based industry are generally driven by knowledge creation capability dependent on human resources, having information sharing and access mechanisms so complementary capabilities can be efficiently exchanged and used becomes key to successful corporate strategy, especially when that knowledge is growing and becoming increasingly diverse.

There is some evidence suggesting when innovation is dependent on trial and error, it is best done when many players try different strategies and are held responsible for the projects they choose (Columbia Engineering Conference on Quality September 1997).

If the large drug companies can successfully form principal-agent relationships with biotechnology companies doing advanced research in a particular area in the same way that Japanese parts manufacturers have with large assemblers, there may be opportunities for major breakthroughs without the drug companies having to put such trial and error processes inside the company where they may be less easy to manage. If the make or buy decision in a science based industry is generally driven by knowledge creation capability dependent on human resources, the basis for new product, i.e. drug development, becomes more dependent on the nature and facility of information exchange between groups and individuals than asset ownership. Creating information sharing and access mechanisms so that complementary capabilities can be efficiently exchanged and used then becomes the key to successful corporate strategy in knowledge based industries, especially when that knowledge base is growing and becoming increasingly diverse as in the ethical drug industry.

Another information sharing issue related to biotech is pharmacology. Classical pharmacology models are often irrelevant for biotech-based drugs. While some proteins express their activities across other species, others can be more species specific. Neither poor results nor good animal trial results need be predictive for humans. Particularly difficult problems are those related to toxicology since some animals develop neutralizing antibodies (Harris 1997). Technical support systems are important in biotechnology as well. One is transgenic animals. They provide information on the contribution of particular genes to a disease. This is done by inserting genes that have the function of expressing the phenotype, or interbreeding heterozygotic animals to produce “knockout animals” that suffer from inherited metabolic diseases. Transgenic animals are relevant to early phase clinical trials since the data from these animals contribute useful data on dose-selection

and therapeutic ratios in human studies. In addition, they offer hints to which variables are secondary. This simplifies the clinical trial design. In general, significant input in the design and running of phase I and II trials must come from the bench scientists who built the molecule (Harris 1997). Since clinical trials for biotech drugs lack clear guidelines, in-house communication among drug discovery, preclinical and clinical trials is important, especially due to the increased use of transgenic animals bred to examine inherited diseases. This process in phase I/II trials can be greatly facilitated by information sharing technologies and acts as another driver towards a more integrated approach to decision making using IT.

### **Structure-Based Drug (“Rational Drug”) Design**

This is also true of structure-based drug (“rational drug”) design or molecular modeling which is a range of computerized techniques based on theoretical chemistry methods and experimental data used either to analyze molecules and molecular systems or to predict molecular and biological properties (Cohen 1996). Traditional methods of drug discovery consist of taking a lead structure and developing a chemical program for finding analog molecules exhibiting the desired biological properties in a systematic way. The initial compounds were found by chance or random screening. This process involved several trial and error cycles developed by medicinal chemists using their intuition to select a candidate analog for further development. This traditional method has been supplemented by structure-based drug design (Cohen 1996) which tries to use the molecular targets involved in a disorder. The relationship between a drug and its receptor is complex and not completely known. The structure-based ligand design attempts to create a drug that has a good fit with the receptor. This fit is optimized by minimizing the energies of interaction. But, this determination of optimum interaction energy of a ligand in a known receptor site remains difficult. Computer models permit manipulations such as superposition and energy calculation that are difficult with mechanical models. They also provide an exhaustive way to analyze molecules and to save and store this data for later

use or after a research chemist has left. However, models must still be tested and used and eventually, chemical intuition is required to analyze the data (Gund 1996). Then the drug must proceed through animal and clinical trials.

Still the idea behind this modeling is the principle that a molecule's biological properties are related to its structure. This reflects a better understanding in the 1970s of biochemistry. So rational drug design has also benefited from biotechnology. In the 1970s and 1980s, drug discovery was still grounded in organic chemistry. Now rational drug design provides customized drug design synthesized specifically to activate or inactivate particular physiological mechanisms. This technique is most useful in particular therapeutic areas. For example, histamine receptor knowledge was an area where firms first took advantage of rational design since its underlying mechanism was understood early (Bogner and Thomas 1996). The starting point is the molecular target in the body. So one is working from demand rather than finding a use for a new molecule.

The scientific concepts behind this approach have been available for a long time. The existence of receptors and the lock-and-key concepts currently considered in drug design were formulated by P. Ehrlich (1909) and E. Fischer (1894). Its subtleties were understood, though, only in the 1970s with the use of X-ray crystallography to reveal molecular architecture of isolated pure samples of protein targets (Cohen 1996). The first generation of this technology conceived in the 1970s considered molecules as two topological dimensional entities. In 1980s it was used together with quantitative structure-activity relationships (QSAR) concepts. The first generation of this technology has proven to be useful only for the optimization of a given series (Cohen 1996). The second generation of rational drug design has considered the full detailed property of molecules in the three dimensional (3-D) formula. This difference is significant, since numerical parameters in the QSAR approaches do not tell the full story about the interaction between a ligand and a protein (Cohen 1996).

This has been facilitated by software and hardware becoming less costly. Thus many scientists are paying attention to computational techniques that are easier to use than mechanical models. This underscores the role of instrumentation in scientific research stressed by Rosenberg (1994). Availability of new instruments, including computers, has opened new opportunities in technological applications and furthered research in new directions. Three dimensional graphics particularly suits the needs of a multi-disciplinary team since everyone has different chemical intuition but appreciates the 3-D image. Rosenberg (1994) notes scientists who move across disciplines bring those concepts and tools to another scientific discipline such as from physics to biology and chemistry. This suggests the importance of sharing instruments, particularly computer images and databases that help people work and think together.

The predominant systems of molecular modeling calculations are UNIX workstations, particularly three dimensional graphics workstations such as those from Silicon Graphics. But other hardware such as desktop Macintoshes and MS-DOS personal computers on the low end and computer servers and supercomputers on the high end have been used. Computational power is required for more complex calculations and this guides the choice of hardware. A variety of commercial software packages are available from \$50-\$5,000 for PC-based systems to \$100,000 or more for supercomputers. Universities, research institutes, and commercial laboratories develop these packages. Still, no one system meets all the molecular modeler's needs. The industry therefore desperately needs an open, high-level programming environment allowing various applications to work together (Gund 1996). This means those who for strategic reasons want to take advantage of this technology must now do their own software development. This is the competitive software compulsion facing many drug producers. In turn, the better they can select systems, develop their capabilities, and manage their use, the more successful they will be in drug development and in managing other aspects of the drug pipeline.



The choice of hardware is based on software availability and the performance criteria needed to run it. Current major constraints are the power of graphics programs and the way the chemist interacts with the data and its representation (Hubbard 1996). Apple computers have frequently been used in R&D because of superior graphics, though this edge may be eroded by new PCs using Pentium MMX as well as moves to more open systems. However, Dr. Popper, Merck's CIO, feels that the real issue, is the software packages for the MAC that research scientists know and rely on but that are not yet available for Windows NT. Thus, MACs continue to be used for Medical R&D which keeps the Windows market from developing. There are, in addition, the elements of inertia, emotional attachment and training which are apparent at major medical schools too.

In sum, rational design has opened a wide range of new research based on a firm's understanding of biochemical mechanisms. This means tremendous opportunities to enter new therapeutic areas. However, since rational design is very expensive, it has raised entry costs and the minimum effective size for pharmaceutical firms by putting a premium on those with a sequence of cash generating drugs. It also has favored firms with broader product lines able to spread the costs of equipment over many projects and to transfer knowledge across therapeutic areas, contributing to the increased cost of new drugs through higher R&D and systems support spending (Bogner and Thomas 1996).

A similar analysis applies to the use of other new technologies because major U.S. and Japanese companies to discover and develop drugs systematically, such as combinatorial chemistry, robotic high-throughput screening, advances in medical genetics, and bioinformatics. These technologies affect not only R&D but also the organization and the way they deal with other organizations as many new technologies are complementary. For example, high-throughput screening automates the screening process to identify compounds for further testing or to optimize the lead compound. Thus, both regulatory and technological change have raised the advantage of developing innovative drugs, even

though it is inherently risky and forces firms to develop better skills in using information technology to support the process.

### **The Pharmaceutical Industry in the United States**

As explained above, healthcare and the pharmaceutical industry are closely intertwined, especially in the U.S.. Ever since the election of the Clinton Administration, U.S. healthcare has been the focus of heated debate. The pricing of pharmaceuticals in particular is one of the most controversial aspects of the industry. Estimates of the cost of bringing a new drug to market are up to over \$250 million (DiMasi et. al. 1991). However, once drugs are on the market, the costs of manufacturing, marketing and distribution are relatively small. This loose connection between marginal cost and the market price seems to require further justification for drug pricing.

While the obvious answer lies in the high fixed cost of drug development and the expensive and time consuming approval process prior to any positive cash flow, the answer is still not easy. Furthermore, the drug market is very complex for several reasons. First, there are many drug classes for which only a few products exist. Secondly, HMOs (health maintenance organizations) and other managed-care plans can negotiate substantial discounts because they are able to control the prescription decisions made by their participating physicians and because they buy in large quantities. These health organizations are highly price sensitive. This means drug prices are substantially determined by the purchaser's demand elasticity. This demand in turn determines investment decisions (Schweitzer 1997). Thirdly, the market for pharmaceuticals is highly segmented, both domestically and internationally, and price discrimination between and within national markets is common. Research studies cannot even agree on a common measure of wholesale price. Indeed, no measure captures actual transaction prices, including discounts and rebates (Schweitzer 1997). Fourth, consumers do not have enough scientific knowledge to assess different drugs. Thus, gatekeepers such as doctors are important (Hirsch 1975).

Yet, the current trend is towards managed care and HMOs who closely control costs. This development clearly indicates physicians are losing some autonomy in drug selection. Thus it is not surprising the market share of generic drugs has increased from 15% to over 41% between 1983 and 1996. This has forced the ethical drug manufacturers to communicate both more effectively with the HMOs and managed care organizations in addition to physicians and to demonstrate the improved efficacy of their products as compared with generics. The acquisition of PBMs (pharmacy benefit managers) by pharmaceutical companies is an important development in this regard. Physicians now have to prescribe drugs available in the formularies of the managed-care organization. PBMs suggest cheaper alternatives to physicians for a given therapeutic benefit to save money. Eighty percent of the 100 million patient/member PBM market as of 1993 is controlled by the five big PBMs (Schweitzer 1997). In turn, when PBMs and mail-order companies expand, the small pharmacies lose the data necessary to examine various drug interactions. Since current U.S. law protects the propriety data of pharmacists and pharmacy chains, information on prescription for those patients who use pharmacies and mail-order companies actually becomes fragmented. It is likely this development could affect pharmacists' jobs as well.

A fifth reason is FDA approval does not mean new drugs are better than old ones. As noted above, this has pressured drug companies to prove the effectiveness in cost and quality of life their drugs bring to patients. Recently, drug companies have often tried to show how their drugs can help patients restore a normal quality of life. As already described, these concerns complicate the design of clinical trials. Consolidation among wholesalers, the greater complexity of clinical trials and globalization favor firms with substantial resources and are part of the reason for the industry's merger trend, especially between U.S. and European companies. The leading pharmaceutical firms ranked by 1994 sales are as follows (Scrip Magazine, Jan. 1996), with five of them the result of cross border mergers. Merck ranks 2d:

<b>1994</b>	<b>1993 (*1)</b>	<b>Company</b>	<b>Pharmaceutical Sales (*2) (Million Dollars) (*6)</b>	<b>Increase from the previous year (*3) (%)</b>	<b>Share of Pharmaceutical Sales in Total Sales (%)</b>
<b>1</b>	2	GlaxoWellcome (UK)	12,223.9 (*4)	-	100.0
<b>2</b>	1	Merck (U.S.)	9,416.3	7.3	62.9
<b>3</b>	4	Hoechst-Marion Merrell Dow (Germany)	9,351.7 (*4)	-	-
<b>4</b>	7	American Home Products (U.S.)	7,425.0 (*4)	-	55.0
<b>5</b>	3	Bristol-Myers Squibb (U.S.)	6,970.0	6.8	58.2
<b>6</b>	9	Roche-Syntex (Switzerland)	6,421.3 (*4)	-	42.3
<b>7</b>	6	Pfizer (U.S.)	5,811.2	13.3	70.2
<b>8</b>	5	SmithKline Beecham (UK)	5,532.2	5.8	59.5
<b>9</b>	-	Pharmacia Upjohn (U.S.)	5,304.0 (*4)	-	78.0
<b>10</b>	8	Eli Lilly (U.S.)	5,248.0	10.3	91.9
<b>11</b>	11	Johnson & Johnson (U.S.)	5,158.0	14.9	32.8
<b>12</b>	13	Takeda (Japan)	4,856.7 (*5)	15.5	64.3
<b>13</b>	10	Sandoz (Switzerland)	4,840.5	5.8	41.7

□

\*1: Rankings of GlaxoWellcome and Hoechst-Marion Merrell Dow in 1993 depend on Glaxo and Hoechst, respectively.

\*2: Conversion to U.S. dollars is based on the average exchange rate in 1994.

- \*3: Comparison is based on U.S. dollars
- \*4: Calculation based on the sales of companies before mergers
- \*5: Including OTC (over the counter drugs)
- \*6: Excludes sales through strategic alliances

## **Merck**

Merck is a multibillion dollar pharmaceutical firm with a long history going back to the 19th century in the U.S. and the 17th century in Germany. While in the past they have diversified into areas like animal health care, they are now very focused almost exclusively on human health, in particular, on ethical branded prescription drugs within human health care since they have found this is their most profitable business area. Also, given the many opportunities that exist, it will demand all their capital and energy for the foreseeable future. It has therefore spun off its animal health care business to a joint venture and sold its specialty chemical business. This strategy and motivation is similar to Takeda's focus on human health, whose market is more lucrative than its other businesses. The company appears to stress their ability to bring innovative drugs to market. Merck briefly tried to produce generic versions of their drugs, but found it was not worth the investment. In addition, they now assume someone else will produce their OTC (over the counter) versions too. This strategic focus is now underscored by their active formation of strategic alliances.

For example, in the OTC medicine market in the U.S. and Europe, but not in Japan, Merck relies on Johnson & Johnson through a joint venture with J&J to market, distribute and sell the OTC versions of Merck's prescription drugs. This means Merck has seen the OTC market as one way to lengthen the revenue stream for some of its products after their patents expire. In Japan, Merck's agreement is with Chugai Pharmaceutical Co. Ltd. They formed a joint venture in September 1996 to develop and market Merck's OTC medicines there (Merck 1996 Annual Report). Moreover, Merck and Rhône-Poulenc have announced plans to combine their animal health and poultry genetics businesses to form

Merck, a new company that will be the world's largest in animal health and poultry genetics (Merck 1996 Annual Report).

Their primary strategic focus on ethical drugs seems appropriate, but as explained above it is also critical with respect to this strategy that they maintain relationships with those in scientifically related fields. Their work with Rhône-Poulenc must be examined in this light since improving their competence in the genetic business seems a good part of their strategy given developments in biotechnology and the Human Genome Project. This is because biotechnology-related drugs are often species-specific (Harris 1997). More knowledge about the genetic make-up of human and animal bodies may provide some insights into the appropriate choice of animals in pre-clinical trials from which to extrapolate observations to humans. Since this extrapolation is never perfect and you have to do animal experiments anyway, they have added to their competence in genetics via a joint venture with Du Pont called Du Pont-Merck Pharmaceuticals Co, whose investors are E.I. Du Pont (50%) and Merck (50%). This firm has capabilities in fermentation, genetic engineering/rDNA, cell culture, hybridoma, protein engineering, and tissue culture. By forming this alliance, Merck was able to exchange its strengths with Du Pont, an early investor in biotechnology. Du Pont-Merck Pharmaceutical has also developed its own drugs in cardiovascular disease.<sup>7</sup> Like other pharmaceutical companies, they continue to sell their branded products as long as they can once they have gone off patent but at a lower price in order to meet generic competition. Cost conscious HMO's increase this downward price pressure. Yet, according to Merck some demand for the branded product continues once they adjust the price downward. This is due to better quality, consistent dosage, and brand awareness of the original.

Strategically, Merck sees itself as a growth company with a growth target of about 15% per year. This signals a continuing need for cash flow, i.e. from existing drugs, and a

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<sup>7</sup> Merck sold its share to Dupont in 1998 for over \$4billion, apparently due to its ability to manage more drugs itself.

constant flow of new drugs, i.e. from R&D. They need this growth to continue to offer their shareholders the return they expect and to attract the personnel they need to develop drugs which is their corporate mission. Their products now cover 15-16 therapeutic categories. In five years this will expand to between 20 and 25 categories depending on the success of various stages of drug testing. Important new products in the pipeline include Singulair for asthma, Aggrastat for cardiovascular disorders, Maxalt for migraine headaches, and VIOXX, an anti-inflammatory drug, which works as a selective inhibitor targeted at rheumatoid arthritis. They are in phase III trials for all of these new drugs. Propecia for male pattern baldness recently received FDA approval.

Merck's R&D is done internationally. To avoid duplicate investment, each research center tends to be focused. For example, the Neuroscience Research Centre in the United Kingdom focuses on compounds which affect the nervous system. Maxalt was developed in this Centre. The one laboratory in Italy studies viruses; while the one laboratory in Tsukuba, Japan (Banyu Pharmaceuticals) emphasizes the circulatory system, antibiotics, and anti-cancer research (Giga, Ueda and Kuramoto 1996). This concentration pattern often reflects the comparative strengths in R&D and the therapeutic demand structure in each local market.

Still, selecting the appropriate R&D projects while critical to their success is very difficult. This is because no discipline in science has as blurred a distinction between basic and applied research as biotechnology. The distinction is usually not well-defined because applied research often contributes to basic research. Indeed, in molecular biology, science often follows technology. Still, as a general approach, Merck tries to focus on applied research and development rather than basic science. They rely on universities and smaller biotech firms for the later. However, they do some basic research. For instance, they did basic research related to AIDS, and it was from this they developed the protease inhibitors that are now a basic part of AIDS therapy. Their approach is to gather information from published and ongoing research in various life sciences and to then look for solutions.

Since they need a return on their investment in R&D to stay in business, a potential solution has to have a market big enough to justify further investment. If it has therapeutic potential but not a large market potential, they will usually get another entity to pursue it. Smaller companies who do not see much chance in competing head-on with major companies tend to pursue drugs with smaller market potential.

As part of their R&D drug evaluation process, Merck also recognizes that even if it is the first to market, someone else may produce drugs in the same therapeutic area. This is because the basic research is available to anybody else who is also tracking basic science. If these competitive later drugs are superior in terms of efficacy and cost effectiveness, the second drug to get FDA approval can in fact win the market race. For this reason, from a strategic viewpoint Merck has organized a designer chemical group to modify and optimize the chemical once a compound has been identified as working. This strategy is also partly driven by the cost containment movement in major health care markets. Since today's healthcare providers analyze the cost effectiveness associated with drugs, ones that are less troublesome to administer are preferred. This is because long term treatment cost depends on how easily patients follow the prescription and how often nurses have to assist them.

In addition to efficacy, there are two other important issues in drug development: bioavailability (the rate and extent to which a dose actually reaches its destination in the body) and safety. To get such good results, information technology plays an important role. The first is in regard to molecular modeling. They design particular molecules meant to achieve drug-receptor binding. (As explained above, the "key and lock" complementarity between a drug and a biological receptor in our body was suggested in the early 1990s.) Merck then combines this information with data mining. They have a library collection of chemicals they have discovered that includes about one million items. Associated with each chemical is a description and information about it, including the results of any animal or clinical studies plus side effects. When they identify a new



molecule, using the computer and search-engines, they then look for similar molecules or chemicals they have already discovered or know about. This gives them some idea what the new molecule might do or what they should examine further, including safety issues.

For example, their development of AIDS drugs involved 32 possible versions of the same chemical molecule. Without the computer it would have been very difficult and time-consuming if not impossible to analyze and screen them one by one. However, it was possible to do the screening rather efficiently due to the computer's ability to visualize and display complex three-dimensional structures. This technique as outlined above is often called "rational drug design," although some scientists prefer to call it structure-based drug design. This is because the new method has its weaknesses and cannot substitute for an older method, sometimes called "random drug design".

Merck also uses information technology methods based on combinatorial chemistry. This method is becoming more popular among other major pharmaceutical companies too. As already explained, combinatorial chemistry speeds up the process of generating novel leads and optimizing previously known leads. This improvement is important since synthetic chemistry traditionally took time and had limited efficiency. This new method involves a large library of compounds from which they generate mixtures of the compounds in the library. This is a very large interactive data base management system.

Under this system, biologists develop a set of assays which conform to a particular standard from certain biological surrogates which they use to test the efficacy of the molecule with respect to a certain disease. They can run a high volume of molecules and tests in this way. This is called high-throughput screening. Since they have libraries of similar assays kept in a standard way, they can do a lot of computer based testing using algorithms which would suggest likely results before moving to animal testing. The idea behind this is that similarity in action often suggests similarity in mechanisms of action, mode of resistance, and molecular structure. To ensure consistency across tests, they have

established various repeatable procedures. Thus, the computer, software, the organized data bases, and the established procedures are highly complementary. Not only this but the recent developments in science such as genomics and biotechnology and the transformation of the market all underlie Merck's strategy of expanding the therapeutic areas quickly. Still, according to our contact at Merck, no single technology would determine their R&D trajectories. Rather, it requires a complex mix of talents covering not only R&D but also marketing and manufacture, finance, corporate development, and information systems.

For this reason, their R&D process begins with a contract with a development team. The contract covers who is involved, what resources are needed, and a timetable. If it is clear even after a month that the contract is not being met, there will be a review and either the contract will be adjusted or the project will be terminated. The success of the laboratory is measured by how many compounds can be marketed. But this is dependent on successful drug selection. Therefore, the choice of what to pursue and what not to pursue is the most important decision they or any drug company can make and it is the ability to manage this process effectively that will determine corporate success. For every potential candidate compound, they have to do an economic analysis. This is why manufacturing and marketing people are on the initial contract assessment review panel in addition to the top R&D people. That is, it does not make sense to pursue a solution to a disease unless there is a strong potential for drug development and a very large market potential to justify the commitment of resources. After this decision is made, there is a series of stage reviews to constantly check on the performance of the R&D process. The review focuses on the probability of success and the payoff if one is successful. Difficult projects are sometimes chosen because Merck knows other companies will face similar difficulties in developing such drugs.

Some types of drugs are more costly than others to manufacture or to conduct clinical trials. The review process takes these factors into account. The cost difference in

the latter case comes from the difficulty of proving effectiveness. For instance, it is relatively easy to show the effects of a drug for infectious diseases in comparison to a drug for cancer or heart disease. Anti-cancer and cardiovascular drugs require long-term observation and more patients need to be involved in the trial. It is not unusual to have 4000-5000 patients over a 5-6 year period. This necessitates tremendous data gathering and data management and is thus an important aspect of their IT strategy.

Further, since HMOs now demand cost effectiveness in addition to efficacy, pharmaceutical companies have responded by doing outcome research. For example, they try to show how their drugs will help patients to go back to work as soon as possible. Although getting this kind of information from the outset is cheaper than adding it later, it still costs them more money through added complexity. It is also a political process as we have seen in the pressure of AIDS activists on the FDA to speed up the drug approval process for related treatments.

Merck is well known for their ability to effectively design clinical trials to satisfy FDA requirements. This core competency has contributed to the relative efficiency with which many new drugs developed by Merck have received FDA approval in recent years (Gambardella 1995). In particular, they believe it is important to design effective clinical trials which have good statistical power. Before any clinical trial, they develop a protocol which defines the variables to be measured and how they will do it. It covers what types of patients will be included in the study, what dosage they will be given, how the controls will be managed, and the measurement criteria. Clinical trials are very costly and represent roughly one third of the cost of developing a new drug. There is thus a stage review at the beginning of the clinical trial and as the trial reaches various milestones.

To improve the quality of the clinical trial data they have also supplied PCs to the investigators and have had them input the data directly rather than waiting for their own people to gather results. This speeded up the data entry process and made the investigators more aware of the data entry process. However, Merck found not all the

data were consistent and that they had to do a lot of cross checking. Therefore, they now send their own Merck people with laptops into the field to enter the data directly from the patients charts. The people at Merck sponsoring the trial are responsible for gathering accurate data. They have found it is cheaper fixing the data at the collection point than trying to adjust it later. In fact, the cost of fixing it goes up by a factor of ten at each subsequent stage. This approach has had the added benefit of putting the clinical trial data collection on a real time rather than on a batch basis as in the past. This has proved a real benefit since companies are now under pressure in clinical studies to find centers that can deliver the highest quality data in the shortest time. This is because the opportunity cost and revenue impact of faster study execution and higher data quality is so high when it achieves FDA approval and thus marketing revenues more quickly. Under these circumstances the direct cost of gathering the data directly is a secondary matter (Hovde 1997) compared to quickly receiving FDA approval. This is a clear case of how total cost analysis can justify the development of a customized information subsystem provided the proper analytics and decision making criteria are in place.

Manufacturing has also become more strategically important. Merck used to try to have enough product to supply the customer what they needed. Now they analyze whether they are the only source for a drug or if a customer can easily get a similar drug or a generic version from a competitor if Merck does not have enough product on hand. Through this process they hope to reduce expensive inventories. This is because their drug production process is primarily a batch process. Thus, they and others in the industry have generally produced enough supply for several weeks, and then cleaned the plant to produce another drug. This manufacturing approach when combined with full availability for all drugs builds inventory and cost. They have therefore moved away from this supply structure even though supply chain analysis, such as just-in-time production, is not amenable to their production system. Rather, what they have done is to break the manufacturing process into three separate stages which they manage.

These stages are (1) bulk manufacture of the pharmaceutical ingredients, (2) the formulation of the product, i.e. transforming the active ingredients produced in the first stage, and (3) packaging. There are two basic approaches to the first stage. One is to use special purpose equipment; the other is to use flexible equipment. The latter approach involves cleaning plants to switch the chemical ingredients, which tends to lead to large inventories and puts pressure on production capacity as they try to expand the number of therapeutic drugs they are marketing. Even though Merck has 30 plants world-wide, because of environmental regulations, getting new plants in the United States is becoming more difficult. This partially explains their decision to get out of generics. But in any case it means they need to get as many drugs produced in their existing plants as possible. This has led to greater emphasis on special purpose equipment that allows them to shift production more easily between products reducing inventories and cycle times.

They have also taken another approach which is to make the new drugs stronger so their one day dosage is smaller in volume. Thus, capacity becomes less important as they get more pills from a given output. Further, most drugs require four to five stages and some requires seventeen steps to produce. To make the production process efficient, it is therefore desirable to reduce the number of production stages. In general, going through more stages reduces the amount of output from a given amount of input (Fukao 1994). In addition, the cost of handling intermediate goods at each stage adds to production costs.

Merck now uses information technology to control and manage these aspects of the supply chain, thus extending their move towards “controlled production” where every aspect of drug development, production and delivery is monitored and controlled including after sales side effects. In manufacturing, they use CIM (Computer Integrated Manufacturing) where the entire factory is linked together under centralized control. Their approach is “the best of breed” approach. They try to buy the best package available that meets their requirements. However, the integration of these into a total manufacturing

system or suite to produce the product in the most cost effective way is their own proprietary middleware system which they developed. That is, they developed a set of tools needed to integrate Merck's manufacturing system and services. Dr. Popper felt Merck's approach was different from Takeda's whom they had visited and who he said were impressive. They licensed the system to Logica, but it never sold. This attempt at marketing the product was to reduce the continuing cost of support.

Nevertheless, even without external sales, Dr. Popper was convinced they got full value for both the packages they bought and the integration system they developed. This is because they subject the selection of software and IT (Information Technology) projects to the same contract/review discipline they use in developing drugs. They use IT to help control business processes. In fact, IT people are intimately involved in this process from an organizational as well as an operations standpoint. For example, Dr. Popper sits on several of the contract evaluation committees. They have now forced the marketing and manufacturing people to work together. This has been successful since each function recognized they needed to solve the same problem. Since Merck's organizational reengineering group also reports to Dr. Popper, it is easier for him to achieve this type of integration and monitor its performance.

In their tabletting plant in England for instance where they have their most advanced CIM operation, they have now moved to a paperless operation but with regular interfaces top to bottom with other plants that are supplying them with bulk chemical formulations. In this process, they have reduced their cycle times from 2 weeks or one month to 5 days. They are almost ready to produce to order. Unfortunately, they have only been able to do this for tablets so far but they are moving towards trying to do it for all plants. Even after mass-scale production starts, plant workers contribute significantly to reducing the operating cost. This requires good detailed understanding of the underlying process and information sharing. Furthermore, all processes eventually get into trouble.

Local engineers have to interpret the information and act on it. So, good data systems such as “process data management systems” are needed.

Merck also saved over \$400 million through its procurement re-engineering project. Since Merck is a very big company covering many regions and functions, it is difficult to track and coordinate all the transactions both inside the company and with other companies. The team tried to reduce the number of global suppliers from 40,000 to 10,000 and to consolidate the product volumes purchased such that Merck could improve its bargaining power and increase the percentage of firms under contract from 20% to 80%. To achieve this goal Merck developed customized data structures and decision support systems. While they could use some commercial software packages, to get full functionality and impact, they had to create their own messaging system to integrate procurement with other activities. As the basic procurement module, they chose SAP's R3 procurement module based on its architectural flexibility, scalability, functionality and the supplier's global support capabilities since Merck needed to implement the system worldwide.

The new system helped Merck to order electronically and reduce paperwork. This created order information that could be used for budget approvals. In addition, the decision support system provides employee customers with opportunities to ask questions about procurement data, and they can now find savings opportunities through access to this database. To integrate the SAP module with Merck's other computer applications, Merck developed a “telephone switch” technology. Merck used a set of middleware products they purchased and integrated themselves since they needed to be aligned with their own unique systems and organizational structure. The switch is the Transaction Data Manager from Century Analysis, the store and forward product is MQ series, now from IBM. This switch also performs a translation from the language of a “sending” application to the language of the “receiving” application. The local language of the sending application is translated into a “neutral” language, “Merck Common Business Language.”

By putting this common language in the middle, Merck reduced the number of translations required between local languages effectively speeding and facilitating the exchange of information. In effect, Merck solved an information engineering problem so that they could quickly reconcile the kinds of information one application needs to send to or receive from other applications. This integrated information can then be stored in data warehouses to support various computerized decision systems.

They have also attacked inventory control more directly. They have joined the North American Supply Chain Project, which involves U.S. marketing and manufacturing sharing responsibility for the availability of certain drugs. Desired level of inventory differs from drug to drug. Since pharmacists may switch to different brands for a patient if you do not keep a certain level of inventory to supply the pharmacies continually, Merck previously kept inventories at levels in various geographic centers that enabled them to fill 98% of pharmacies' orders. Now, as explained above, they do a more sophisticated calculation using internal formulas to manage and target the percent they want to fill over a wider range. They set sales targets and then assess whether a competitor in the North American Supply Chain Project would take the order if they did not fill it. Interestingly, this kind of order management (ERP/MRP) has reduced the number of backorders below their targeted measures and has lowered inventories while actually increasing availability. This result has surprised them but seems to be due to the fact that to keep their own inventories low pharmacists were doing more switching than Merck realized without ordering more supply. Their interface with their customers are generally standard IS interface protocols. They also get a standard set of data on physician prescriptions (24 months) which is available to all the drug companies.

However, they do have their own established format for this data such that they get this purchased information into a form that is useful to them. Sales representatives carry laptops to target sales and have the prescription information downloaded into their laptops. They then know the prescription habits of the doctors in their geographical area



and also for each type of therapeutic use. The sales representatives can then prioritize their visits to the doctors. In the future, Merck expects even a bigger use of such database marketing which will enable them to compare the performance of a sales representative with his competitors in each region. They also use IT to forecast the demand for new products. This is very difficult, particularly for those products in new therapeutic areas. They thus think they need to find more analytical tools to do their forecasting.

### **Managerial Decision Making**

Merck uses real options analysis in their R&D decision making (Harvard Business Review Jan-Feb 1994). The traditional method of comparing discounted cash flows is misleading since it does not take into account the loss in value from exercising an option and the increase in value from creating an option (Dixit 1995) when an option is understood as the right but not the obligation to pursue a business opportunity. Thus the option itself has a positive value which should not be ignored.

When projects require committing resources that cannot be transferred to other purposes, it is often beneficial to wait and observe more about the project. Such waiting without giving up the right to pursue the project has value since one can avoid expenses today when some future event may indicate against continuing. Similarly, the present discounted value of undertakings which create new options also tend to be underestimated since they give the added benefit of future flexibility to pursue projects only when the future profitability of those projects seems more certain. Pharmaceutical R&D offers ample opportunities for using such decision making criteria. This is because drug companies compete in a market involving many uncertainties. For example, R&D sometimes benefits from new scientific findings that occur in the middle of a project. Yet, given long product lead times, to bring drugs to market first it is often necessary to start R&D projects that only appear likely to generate many attractive options in the future. This situation fits well with this kind of option analysis. Merck also uses this analysis in hedging against foreign exchange fluctuations using derivatives and long-term foreign

exchange futures as well as in evaluating acquisitions of other companies. Merck's CFO Judy Lewent acknowledges support from senior executives and other divisions in introducing the Monte Carlo simulation (CFO 1994) for these purposes.

Since Merck has considerable data on their past successes and failures in R&D, they can use this and other information such as the stock price of a competing biotech company to value an investment in a particular drug or therapeutic solution. They have adopted this method because accounting rates of returns are upward-biased measures of the true profitability of R&D investments. This result follows from the fact that accountants treat R&D as an expense rather than as an investment. This method understates the value of pharmaceutical companies' assets in a R&D project and overstates their rates of return (Myers and Howe 1997). Furthermore, it does not consider the fact that as an R&D project progresses, the project risk declines. Therefore, to calculate the present value and the return to investors, a Monte Carlo simulation is used to predict these values under different scenarios. Each scenario is generated from a unique set of random draws from probability distributions based on the odds of a drug's discovery, survival and commercial success profile. Since R&D decisions are sequential, the real options analysis takes into account the flexibility of not making a commitment (sunk investment) as having value. Senior managers use this Monte Carlo simulation in their decision making. Another use is in managing the contingent progress payments to smaller companies or university research. After giving money upfront, the company has the right not to pursue the project further. The real options analysis is relevant in this regard.

Merck management takes a team approach under CEO Gilmartin to such decision making. He created world-wide business strategy teams, each of which is focused on a key disease. Executives from many functions develop a disease related drug development and marketing strategy in a coordinated manner. He relies on the judgment of specialist

executives such as those in R&D for R&D related decisions but the overall business decision is made by the team (Business Week, November 25).

### **Decision Making on IT projects**

IT functions except for Medco are centralized under Dr. Popper, especially the basic IT infrastructure such as large mainframe computers. At the same time, systems development units are aligned with each business unit and report to the head of the business unit in addition to Dr. Popper. The business units include R&D, manufacturing, and U.S. sales and marketing. Sales units are generally localized while IT and manufacturing can be more centralized. This is because health care markets differ across countries due to local laws and customs. On the other hand, the relevant information about chemical plants are mostly described by numerical data related to their equipment. This type of data favors centralization. IT people work with each business partner to help them implement their functional strategy. To coordinate activities across functions, they have a worldwide business team composed of senior functional managers who analyze the market according to disease categories such as cholesterol lowering drugs. They each conduct stage reviews, including drug safety. Important information is reported to functional heads and the worldwide business team which includes an IT person.

The EDP (electronic data processing) operation at Merck seems fairly large. 750 people are doing software development and its EDP (electronic data processing) operation has 350 people working on infrastructure and support. Merck does not have its own captive software suppliers. They do 60% of the software development internally and purchase 40% of their software from unrelated companies. They develop core software products for clinical trial systems, basic research, sales force automation systems, and data warehouse applications. They buy financial, human resource, and MRP software from outside. Dr. Popper does not think client servers and office computers combined with work stations and PCs will replace the mainframe. This is particularly true for

manufacturing class servers where they need the greater mainframe speed and capacity. Further, they expect to use supercomputers indefinitely in their basic research.

The project approval committees (PAC's) are also involved in the business review process for IT projects and apply the same selection methods and criteria as they do for drugs since an investment in an IT project means less money available for investment in a new drug which is their basic business. Thus, at each stage people who are responsible for the project sign a contract. This process starts with an analysis of the project's conceptual feasibility. Then, they assess the project's order of magnitude in terms of cost and benefits using measures of both money and/or quality. This detailed analysis identifies costs and benefits with allowances for margins of error of +/-25%. This leads to a contract with the project team. One of Dr. Popper's responsibilities is to manage this portfolio of IT projects.

The analysis looks at the IT project portfolio through a bubble chart that categorizes projects into four types in terms of risk and benefit with bubble size indicating the cost or resources committed. These are high risk and benefit or impact. Such projects usually require new inventions or systems. There are low benefit and high risk, which are to be avoided while the best are low risk and high benefit. The latter are often found through a combination of packaged and customized software where many bugs have already been sorted out in advance. IT maintenance including upgrades is low impact-low risk.

	Low Risk	High Risk
High Impact (Benefit)	High Impact, Low Risk	High Impact, High Risk
Low Impact	Low Impact, Low Risk	Low Impact, High Risk

They use the net present cost over the life cycle of the project to arrive at the size of the bubble. In addition, the PACs do not look at IS in isolation but see them as part of the business system supporting successful product development and marketing. That is, Merck recognizes that the whole system needs to succeed for the IT strategy to succeed. For this reason, they insist each IT project have some metric which is identified and agreed to in advance as part of the contract. This metric specifies what is going to change if the project is successful so they can identify if it was actually successful. Thus, they try to express quality in financial terms. In this regard, they have found that the quality of medical care a drug offers may be identified by consumer surveys and customer satisfaction. Investing in brand name recognition also requires some metric. Thus Merck considers it important to identify such instruments to measure successes as well as failures. This type of planning in numerical terms would make it possible to compare the desirability of multiple projects, taking into account their possible consequences from an organizational viewpoint. Centralized managerial decision making seems necessary to successfully implement such an information technology strategy. It also makes people aware of the externalities across the various functions that IT creates. Since each business function pays for their IT support, the system and data come full circle in that these functions must justify their IT budgets.

Another aspect of controlling information that concerns Merck is their need to have consistency in the terms used to describe particular outcomes. They have found by controlling their IT, they can play a role in increasing quality care by forcing on other firms and medical practitioners an agreement with respect to standards in using the same terms to describe the same things from Merck's perspective. This reflects the fact that in the medical field, there are often multiple classifications of diseases. Merck has developed its own lexicon which is available through a Netscape browser on the Internet for use in clinical trials. This kind of lexicon has helped to create better control and consistency for analytical and measurement purposes. It also means data in the database is collected and

classified in a consistent way which allows for greater compatibility which can feed back into the R&D process. They also use librarians to reclassify the types of diseases if someone else uses other ways of classifying particular diseases in various publications. Current multiple standards at WHO, FDA, etc. make comparability a problem. These are issues that need to be addressed in the future, but to the extent Merck is successful and is able to set standards for how data is gathered and classified, it will clearly give them an ongoing strategic advantage in areas such as drug design, expediting clinical trials, and FDA approvals.

Some organizations do not take full advantage of new IT systems since the new systems sometimes introduce difficulties if they are not compatible with how people work with one another or the system. For this reason, it is important to do advanced research and pilot projects before their introduction. One example of how Merck understands and manages this is their worldwide introduction of a new ledger software system. First, they identified all the customers for the system and then discussed it with these major stakeholders in terms of their requirements. Based on this, they examined a number of packages and asked vendors for discussion and product demonstrations. This measured system functionality against user requirements to see which best fit their identified needs. They interviewed other clients of each vendor to understand their product implementation approach and possible pitfalls. This stage saves money and organization time since software is an “experience good” whose value and shortcomings are only made clear after introduction. Since Merck implemented JDE internationally first, they discussed the product with their affiliates too and then piloted it in U.K. before its worldwide implementation. In addition, all the functions and conditions were tested in a conference room pilot environment prior to going live.

This kind of review, assessment and implementation process is becoming very important as IS (information system) business development costs are rising faster than overall costs while infrastructure costs are rising half as fast. While some of this is due to

the improved cost performance of mainframes and other computers, it is also a problem in that many managers think mainframe time is costless. One of Dr. Popper's current tasks is to explain to them how much it actually costs and to get this included in the appropriate budgets. Telecom costs are going up in line with IS costs, though they may use more in the future if they can figure out how to control all the security issues related to the Internet. Right now they are limiting access.

The critical management issue for Dr. Popper is to put the appropriate system in place for each situation. Since the PACs are the key to this process and achieving this goal, he makes sure there are senior managers on his PAC's. Getting them involved has been a major management and strategic breakthrough. For the same reason, Dr. Popper is strongly against the concept of outsourcing since he believes one is then giving up control over the key information behind the business, and Merck will have to compromise in aligning the appropriate IT system with a given business situation. In addition, if the information system relates to a core business, it may not be safe. For example, an inefficient IT system could make a business more volatile, and transaction volume (trials, marketing) could get out of control. This view is probably similar to Toyota's feelings concerning its Just-In-Time system, although Toyota's system involves more parts and a greater variety of products from the same factory. In Toyota's system, a downstream production unit orders an upstream unit to produce the number of parts that is necessary. Any slack during their production is considered waste while having too much inventory also makes it difficult to discern problems in the system until it is too late.

Further, Merck feels outsourcing IT may not be a reversible decision. This is because it may shift control over important information related to future business needs. If Merck is not aware of that information or does not control how it is gathered and processed, it could constrain its flexibility and responsiveness with adverse strategic consequences. At the same time, some information does seem less strategic and it may be cheaper and more efficient to outsource this. Dr. Popper is helping the new head of human

resources to make this type of calculation, though in evaluating whether to retain control, he makes sure he includes an appropriate cost for the mainframe in terms of incremental cost and time. This is because a previous analysis showed the company saved \$1 million by doing it in-house, but ignored the cost of the mainframe and its supporting systems. He is also monitoring to what extent it makes sense to outsource telecom. His view is that there are probably niche functions in non-core and non-strategic areas where it makes sense to outsource. However, he cannot understand those who rely solely on outside IT resources, since he feels the outside service will not react to the firm's business needs because their people are unable to be involved in the day to day operation of the business. Strategic IT planning is thus a tacit knowledge process in which people must be constantly engaged. So outsourcing definitely must be done on a very selective basis. This shows Merck's make-or-buy decision requires consideration about its future strategic flexibility as well as its ability to monitor the information that drives the business.

### **Joint Ventures**

Dr. Popper noted that full exchange of information was difficult even when they had a formal business partnership. In the case of the joint venture with Johnson & Johnson, for example, they only exchange planning assumptions in the OTC (over the counter) medicine business (packaging and tabletting). The interaction is arm's length. This joint venture does not do research. In the case of Du Pont-Merck, though, where they were doing joint research, he worked with their CIO (Chief Information Officer) to set up methods on projects where they are working together for particular researchers to have access to certain data bases at Merck and vice versa. They used secure ID Token cards and dual firewall systems through a point-to-point lease line to control these Intranet links. In addition, Merck did not integrated their supply chain (marketing, sales, manufacturing, distribution). This shows agreement is necessary for some information to flow across organizational boundaries. Joint ventures in this case appear to be one way to



modulate the disclosure of information between the involved parties for their mutual benefit.

### **Medco Division**

Due to complaints from their competitors as well as government regulatory concerns, the Medco division has its own information systems, and any interconnections are through firewalls to protect the integrity of their competitors' sales information from Merck. But they now share some technical standards, and they have kept the development of their systems parallel so gradually they can erase the differences. Both these actions should over time reduce costs and facilitate the sharing of non-competitive data. For example, they will be able to exchange Merck-related information on patients more efficiently. Dr. Popper was quite explicit however that Medco does not favor Merck over other suppliers unless Medco's recommendation of Merck products is legitimate. Nevertheless, they have gradually been increasing their share of Medco's sales.

Still, they do not have access to Medco's database. This is a key point that has been misperceived by the market. Merck does not get any diagnosis information, and in fact currently there is no standard on how patients records are kept in the United States. In the future, in combination with their lexicon described above, they hope to use Medco as a way to get more detailed and consistent patient data on Merck products than they can currently get from the national prescription database. Ultimately, what they would like at the next stage are complete patient clinical records collected according to agreed standards which would give those records over a 5-10 year horizon. They are making some progress in this area, and this is where Medco could prove helpful. It also illustrates how Merck is using a form of embedded software, in this case prescription data related to their drugs, to develop an interactive data base that can impact all aspects of their business from drug development to sales and marketing, including Medco's own operations. It is also using IT as a way to influence and control their external environment, an aspect of "Controlled Production".

This is because Merck-Medco's mail order business is a powerful marketing tool. It can sell drugs at a lower price than other pharmacies. In turn Merck "mines its terabyte data warehouse to uncover hidden links between illnesses and known drug treatments, and to spot trends that help pinpoint which drugs are most effective for what types of patients." (Datamation 1997). This is how it works. With the help of Medco Data, the organization that provides Merck-Medco with system support, Medco designed a user-friendly system to conduct datamining and OLAP querying against the Medco's database containing some 76 million patient and treatment records. Merck-Medco then spent four years turning this huge database into one of the largest mineable massively parallel data warehouses in the U.S. using an NCR Teradata 5100 database platform. Through this process they managed to clean biases hidden in multiple data sources and standardized conditions, enriching its data by integrating additional data on health trends and drug use. They then combined traditional SQL and OLAP products with a sophisticated GUI (Graphical User Interface) as well as data-analysis algorithms (Datamation 1997). In this way, IT expertise has been useful and instrumental to Merck in asking and answering questions it needs to address to operate successfully in the current and future cost containment environment.

### **Information Technology and Organization**

As we have described above, Merck like other major pharmaceutical firms faces multiple business environments where they must justify the use of their drugs to increasingly cost conscious customers in terms of improved efficacy and benefits at the same time that the development of new drugs is becoming more complex and expensive. Yet, they recognize that only by developing and marketing new and more effective ethical drugs can they grow and prosper. Further, these drugs must be sold globally to amortize their high development costs. To do this efficiently requires sophisticated techniques to acquire and manipulate large amounts of data in a standardized manner at several levels, including R&D, clinical trials, manufacturing, marketing and after sales results.

Therefore, using systematic research data and sophisticated analytical methods successfully in their decision making is critical to their current business and future growth. However, even though the need to use information technology is clear, they believe the basic purpose of these systems is to improve the firms' existing decision-making skills which have been responsible for their current success. That is, using systems should not result in automatic managerial decisions but rather should improve the quality of decisions by enhancing the experience and judgment of managers. Therefore, even though one important role for software is to facilitate better communication, they are also strong believers in face-to-face communication among managers in formulating strategies.

At the same time, Merck does not believe the more information everyone has the better, i.e. that all information should be freely shared among everyone in the firm. Thus Merck consciously tries to create some barriers among non-R&D employees to limit the information flow to those with some need to know. However, they are reluctant to create such information barriers among R&D employees since R&D employees only usually request information when there is a reason, an impulse that can be important to their creative process. Indeed, the use of software provides researchers with the common language in which they think and talk. It is essential for multidisciplinary medical researchers to have a common ground and share a part of their chemical intuition. They thus feel the use of software enlarges and extends researchers' knowledge domains.

How has information technology affected this organization? Although the power of PCs has risen substantially, their information management remains centralized. This reflects the scientific nature of the data. In addition, the ease of upgrading and the need to safeguard their proprietary information favors a centralized approach to software management and development. At the same time, it would appear that the firm has less need for job rotation given they now have more cross-divisional exchange of information electronically and via more cross functional committees. Still, there is a high degree of specialization within this industry and the firm's R&D specialists and managers tend to

stay in their area of expertise throughout their careers. So job rotation for other than general managers is relatively low. Still, by facilitating senior managers' access to information at all levels, the firms have decreased the number of middle managers they require while at the same time expanding the skill base of those that remain and their functional areas of responsibility. Thus they are conscious of the relation of power and information and are careful when introducing new information technology tools about possible changes in the distribution of authority and power among employees. However, their basic approach of using information technology to enhance and improve existing core competencies avoids many of these organizational dilemmas since people can see their effectiveness and the company's competitive situation is improved without the need for substantial reorganization and its accompanying disruption.

This strategy contrasts with companies such as Bayer that use a minmax approach to software use and development which focuses on achieving maximum user functionality for the least cost. Under this system, a firm uses a package if it achieves 80% of the functionality users request but does not evaluate whether the additional 20% represents a critical added value or is important in maintaining a core competency. Also, it stresses centralized IT control more to facilitate upgrades than to develop strategies and allocate resources. They do not support certain R&D functions even when the user may require it to efficiently utilize an historical data base or certain programs which may only be available for a MAC or VAX system. This minmax strategy is supported by a review process that has a check list of 20 to 25 benefits that are evaluated for each IT project, making it difficult to isolate one or two key business factors in terms of IT integration or the enhancement of core competencies critical to the drug pipeline (Track 1997). This in turn makes it difficult to assess the projects ultimate success or failure.

The popular press and many reengineering specialists have stressed that a logical organizational outcome of improved information systems is a flattened organization because it is now easier and more efficient for top management to communicate with

lower levels in the organization, and middle management is no longer required to process information or to manage and set objectives for smaller organization subunits. Being able to eliminate tiers of middle managers in turn saves money and is thus cost efficient. For Merck, information technology has had these direct effects. They see less layers as desirable to make more information available more quickly to management in a rapidly changing market. Each person is now able to process more information and has broader skills than before. However, this has not led to large personnel reductions. Rather, each person's scope of skills has become broader which means a person, such as those managing clinical trials, can accomplish more tasks within an expanding market. Therefore, it was the need for clearer accountability not the impact of more direct communication that was the main driver for Merck's development of a more flattened organization with information technology enhancing and facilitating this strategic decision. It did not stress easier monitoring of subordinates via improved information systems as a principal reason for the move to a more flattened organization.

This result is similar to other responses that indicate that for Merck the role of information technology has been to enhance and extend existing strategies and core competencies rather than to restructure or fundamentally change their organization. At the same time, it is apparent through a creative mix of customized, semi-customized and packaged software that they have created an information system and an organizational support for that system which has significantly improved their competitiveness in a wide number of areas. An important aspect of this has been the interactive linking of various functions that in the past were relatively separate: R&D, the drug approval process, manufacturing, marketing, sales and after-sales service. For example, in the case of Merck the development of standardized data bases and access to patient prescription data has allowed them to better monitor drug use after purchase. This has improved their sales forecasts which has helped manufacturing to reduce production runs which has improved inventory levels and shelf life. Their long run objective of production on demand takes this

development to its logical conclusion. Lower inventories of expensive new drugs reduce costs which in combination with the better information on therapeutic results helps marketing in terms of showing cost conscious HMOs the cost efficiency as well as the efficacy of their drugs. This improves sales which of course helps to finance the drug pipeline. It has also helped R&D more directly in terms of therapeutic activity and results that enables them to work on reducing the side effects of existing drugs plus targeting areas for new drug development.

In turn, R&D can now work on more drugs because the improved information systems Merck has developed to managed clinical trials can now handle as many as 24-25 drugs at a time instead of 16-18 as in the past. This of course improves the chances of having a “blockbuster” drug, spreads fixed development costs over a wider range of products, and extends the therapeutic areas they can address. The latter then allows them to benefit from economies of scope in manufacturing, sales and marketing.

Another information systems benefit linking previously separate functions is the increased complexity of manufacturing the new right-handed and left-handed drugs created through molecular modeling. Some of these manufacturing processes are new and can be patented. In addition, they often require several steps in different manufacturing facilities. Therefore, even when these drugs go off-patent, Merck may be able to retain control for several more years. This extends the traditional life of a drug and justifies concentrating greater research resources to their development while Merck will be able to build their proprietary clinical trial and prescription data base that supports developing drugs through these new design techniques. This will put them farther ahead in terms of this type of drug development and their successful marketing. That is, success, profits and expertise tend to compound.

In the introduction to this case, it was noted a potential new production paradigm might be emerging, one being pioneered by leading companies in industries as diverse as finance, semiconductors and pharmaceuticals. It appears to differ from mass production

which is essentially supply push and where significantly lower costs create their own demand. It also appears to differ from lean production which is more demand pull but with even lower costs than mass production, especially in terms of defects and inventories.

We have called it “controlled” production because the firms using it seem to have organized themselves to access the information necessary to monitor and control all aspects of their business and to then act upon it competitively as a firm. This appears to be what Merck does in their approach to R&D, clinical trials, manufacturing, marketing, sales and after-sales support. Data gathering and control have in turn established several beneficial loops which seem to be self-reinforcing and which directly improve costs, quality and competitive position. This case should therefore be closely examined in this light. Furthermore, to the extent this does represent an important new development, the study team hopes other researchers will examine other leading firms in using information technology in their areas of interest to gather further evidence. This is because the competitive implications for both those using these techniques as well as those who are falling behind could have an impact that goes beyond a single industry such as autos. Rather like mass and lean product did in their time as their use spread to other industries, controlled production should in time affect large portions of the economy.

## **APPENDIX I**

### **Summary Answers to Questions for Merck - Strategy & Operations**

<u>General Management and Corporate Strategy</u>	Yes	No
Has the firm integrated software into their management strategy, including using it to institutionalize organizational strengths and capture tacit knowledge on an iterative basis?	x	
Has the firm succeeded solely on the basis of its software strategy?		x

Does the firm believe some customized software and its close organizational integration enables the company to capture and perpetuate on a more consistent basis certain tacit knowledge and unique corporate features, i.e. core competencies, that account for its continued success in the marketplace with reliability and repetition important elements in their thinking?	x
Is the firm's software strategy successful because it is a well managed company that introduces software innovation when it serves corporate goals for enhancing productivity, inventory management or customer relations within its industry?	x
Does the firm generally meet established criteria as a quality organization such as: effective organizational self assessment, use of project and especially cross functional teams, improving quality outcomes through reducing uncertainty, rapidly diffusing learning throughout the organization including the use of software and information technology, effective implementation of organizational and technical change, facilitating change via evolution rather than revolution or reengineering <sup>8</sup> , emphasizing participatory management, having process excellence, using value added analysis, actively doing benchmarking, constant organizational improvement, commitment to concrete realistic goals, effectively managing a dynamic iterative experimental process through goal setting, training and constant consultation?	x
Does the firm plan in detail for world class operational excellence including the contribution of software and information technology to the allocation of resources?	x
Do their planning systems enable management to make better business, operating and resource allocation decisions, including those related to software and IT, with a link to resource valuation techniques?	x
Do they focus on a small number of priorities, usually three or fewer, with a well defined, cascaded system reaching from the commitment of senior management to the department level with associated metrics?	x
Is the firm a "high performance" workplace for services?	x

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<sup>8</sup> MIT Systems Dynamics Group's September 1997 presentation estimated 70% of reengineering efforts fail.



Is there a heavy emphasis on improving process through using software?

### Industry Related

Are industry economics and competitive dynamics an important strategic driver for the firm and for its use of software and informaiton technology in that IT has been adapted to the firm's particular industry and competitive situation? **x**

Do industry paradoxes exist such as: declining stock prices, manufacturing improvements that create product improvement difficulties, or employees' active product use that retards improvements? **x**

### Competition

Is software a significant and successful input into the firm's competitive performance? **x**

Does the firm explicitly and consciously perceive the implications of their software strategies and use on their competitiveness and business success? **x**

Are there direct links between their software strategies and overall management goals? **x Medco R&D**

Do customers, affiliates, competitors, industry analysts, government officials, industry associations and suppliers perceive the competitive benefits or impact of the firm's use of information technology? **x**

Has the firm gained first mover advantages through successssfully introducing software relate innovations? **x**

### Country Related

In pharmaceuticals does nationality seem to be a causal factor in determining the impact of software on the firm's competitiveness? **x**

### IT Strategy

Is firm a sophisticated software user that consciously designs and implements a software strategy to achieve competitive advantage? **x**

Does the firm utilize several types of software input alone or in combination to achieve competitive advantage? **x Comb**

Does firm's system work to rapidly uncover implementation barriers, including using new or improved software generating cross-functional and hierarchical consensus so measured goals can be achieved? **x**

Is leadership at different levels actively involved in software planning, assessment and deployment with regular progress reviews that link plans, goals, benchmarks, metrics, milestones resources and responsibilities? **x**

Does the system allow for flexibility and innovation as well as change and individual efforts provided they meet goal, planning and metric criteria? **x**

Is there a clear vision making project and new product software selection straightforward and closely related to strategic goals and processes? **x Initial & Phase Review**

Does firm's software strategy involve conscious and clearly defined reliance on customized and semi-customized software in addition to packaged software with specific criteria and goals for selecting each type, and do they have ways to measure this so it knows customized software achieves functional or market gains that justify additional expense, including related costs of integrating customized and non-customized software into a single information system?

x  
Leader

Does firm use option valuation methods to manage uncertain and random outcomes since this appears to be at the software implementation frontiers even among very well managed companies?<sup>9</sup>

x  
Clinical  
trials &  
Medco

Does their strategy include increased use, development and integration of industry and company specific vertical application software and embedded software in its production and delivery processes to improve competitiveness?

x  
Work to  
relate

If firm has an embedded software strategy, is it integrated or interactive with their other software and overall business strategy to affect production, product design or service that improve quality and costs long term?

x  
Feel loses  
contact

Do they favor increased outsourcing of software design and development?

x

Does firm believe large-scale outsourcing by many U.S. companies assumes those firms' information systems development need not be integrated with their business organization and that they view their information systems as generic products best developed by outside vendors who can achieve low cost through economies of scale?

x

Do they feel these firms' approach focuses on the cost side of software and that these firms do not see differences among systems used by their competitors?

x

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<sup>9</sup>Easton, George S. and Sherry L. Jarrell, "Using Strategic Quality Planning More Effectively: Lessons Learned from NSF Project Research," Columbia Business School conference presentation, September 1997.

Do they in turn believe this is a mistake by their competitors that gives them a long-term and sustainable competitive advantage over such companies because they believe outsourcing surrenders a firm's strategic software options since systems service companies have an incentive to develop increasingly standardized products and are one step removed from the company's customers and business? **X**  
Some

Has the firm established software strategy that is open and interactive with its customers and/or suppliers? **X**  
Limited

Has this enabled it to capture information or cost competitive externalities? **X**

### IT Operations

Do participants own goals and are then committed to implementation strategies? **X**

Does the firm embed software into its production and delivery processes with competitive market implications? **X**  
Trials and post-sale

Is software technology tied to high speed telecommunications technology, allowing the firm to track, receive and deliver shipments or services directly or on-line without further handling or processing? **X**

Does it manage the potential risks of extensive use of software or open systems? **X**

Do they work to ensure consistency and reduce programming errors? **X**

Is formal interaction a key aspect of planning and implementation? x

Is firm's system institutionalized and self-reinforcing with good communication and consensus building while software and IT play a role, including preventing retrospective justification or target reduction? x

### Human Resource and Organizational Issues

Does the firm pay close attention to systems training and organizational integration for all employees, reducing errors through improved consistency and staffing efficiencies across the firm since software can confound even routine operations? x

Does certain software require special HR competencies or education? x

Does the firm try to change human behavior to use software? x  
But trains

### Parameter Metrics: such as Inventory, Cycle Times and Cost Reduction

Are goals or targets tightly linked to regularly reviewed metrics with inputs coming from all levels that are often cross-functional, affecting large parts of the organization, e.g., cycle times, on-time delivery, and customer satisfaction? x

Does the firm have standard agreed ways to explicitly organize or manage this software selection process? x

Does the firm have agreed ways to measure and evaluate success in using software to promote business objectives such as unit cost, inventories, lower receivables, market share, model development times, or product pipeline? x  
Varies project

Are IT costs balanced against overall long-term productivity gains?	x
Does firm have methods to ensure increased customization costs result in lower costs downstream so that developing and using customized software makes sense?	<b>x</b> Contract
Has the firm created large interactive databases for automatic feedback between stages or players in production and delivery process? And are these databases constantly being refined and updated on an interactive basis with actual performance results in a real time global environment? What are competitive and metric impacts of this, such as reducing inventory costs and wastage while improving quality of customer service?	<b>x</b> Clinical trials – R&D inventory
Has the firm used software to create beneficial feedback cycles that increase productivity, reduce cycle times and defects, and integrate production and delivery process?	<b>x</b>
Do other firms or analysts have other measures competitiveness or views appropriate industry strategy?	<b>x</b> Bayer
Has firm achieved better than industry growth, superior on-time delivery, improved inventory control, reduced down-time or changeover cycles, reduced product or process defects, fewer recalls, lower warranty claims, an improved product development process, and/or other definite and measurable progress relative competitors?	<b>x</b>
Do the firm's metrics go beyond financial to areas like customer satisfaction, operational performance, and human resources?	<b>x</b>
Does their evaluation system apply to new product development and significant projects as well as to continuous operations?	<b>x</b>

## **APPENDIX II**

### **INDUSTRY AND FIRM BUSINESS DATA**

#### **Merck - Financial Highlights 1987-96**

##### **Products 1996 and Product Sales by Therapeutic Area 1994-96**

##### **Medco Sales 1993-96**

##### **Costs and Expenses 1994-96, R&D Expenditures 1987-96, Capital Expenditures 1987-96**

##### **Consolidated Income 1994-96**

##### **Balance Sheet 1995-96**

##### **Illustrations Integrated Use Information Technology**

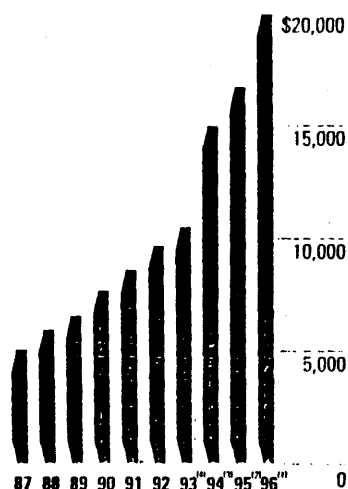
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<sup>9</sup> Easton, George S and Sherry L. Jarrell, "Using Strategic Quality Planning More Effectively: Lessons Learned from NSF Project Research," Columbia Business School conference presentation, September 1997

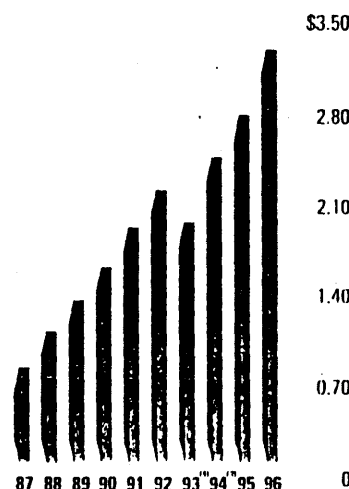
## FINANCIAL HIGHLIGHTS 1987-96 (Merck 1996)

Years Ended December 31 (\$ in millions except per share amounts)	Percentage Change From Preceding Year					
	1996 <sup>(1)</sup>	1995 <sup>(2)</sup>	1994 <sup>(3)</sup>	1996 <sup>(1)</sup>	1995 <sup>(2)</sup>	1994 <sup>(3)</sup>
Sales .....	\$19,828.7	\$16,681.1	\$14,969.8	+19%	+11%	+43%
Research and development expenses .....	1,487.3	1,331.4	1,230.6			
Net income .....	3,881.3	3,335.2	2,997.0	+16%	+11%	+38%
Earnings per common share .....	\$3.20	\$2.70	\$2.38	+19%	+13%	+27%
Dividends paid per common share .....	\$1.42	\$1.24	\$1.14	+15%	+9%	+11%
Average common shares outstanding (millions) ..	1,213.6	1,236.1	1,257.2			
Total assets .....	24,293.1	23,831.8	21,856.6			
Capital expenditures .....	1,196.7	1,005.5	1,009.3			
Net income as a % of average total assets ..	16.1%	14.6%	14.3%			

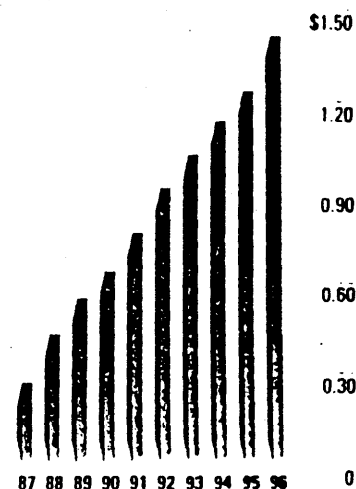
SALES  
\$ in millions



EARNINGS PER  
COMMON SHARE



DIVIDENDS PAID  
PER COMMON SHARE



<sup>(1)</sup> Sales for 1996 were affected by the sales of Kelco and Medco Behavioral Care in 1995. Adjusting for these effects, 1996 sales growth would have been 21%.

<sup>(2)</sup> Sales for 1995 were affected by the formation of a joint venture with Astra and the sale of Syntex (a Medco subsidiary) in 1994, as well as the sales of Calgon Vestal Laboratories, Kelco and Medco Behavioral Care in 1995. (See Notes 3 and 4 to the financial statements for further information.) Adjusting for these effects, 1995 sales growth would have been 21%.

<sup>(3)</sup> Amounts for 1994 include a full year's impact on results of operations of the Medco acquisition and the impact of the formation of a joint venture with Astra on November 1, 1994. Excluding Medco sales of non-Merck products and including Medco sales of Merck products for the full year 1993 to achieve comparability, and adjusting for the effects of the joint venture formation and the sale of the Calgon Water Management business in June 1993, 1994 sales growth would have been 9%. Excluding the 1993 restructuring charge, 1994 net income and earnings per share growth rates would have been 12% and 3%, respectively.

<sup>(4)</sup> Amounts for 1993 include the impact of the acquisition of Medco and a restructuring charge.



# PRODUCTS 1996 AND SALES BY THERAPEUTIC AREA 1994-96 (Merck 1996)

PRODUCT	INDICATION	PRODUCT	INDICATION
<b>AGGRASTAT</b>		<b>CLINORIL</b>	
<i>Aggrastat</i> * (tirofiban hydrochloride)	Unstable angina	<i>Clinoril</i> * (sulindac)	Arthritis
<i>Aldomet</i> * (methyldopa)	High blood pressure	<i>Dolobid</i> * (diflunisal)	Arthritis and pain
<i>Cozaar</i> * (losartan potassium)	High blood pressure	<i>Indocin</i> * (indomethacin)	Arthritis
<i>Cozaar</i> * (losartan potassium)	Heart failure	MK-966	Arthritis and pain
<i>Hyzaar</i> * (losartan potassium and hydrochlorothiazide)	High blood pressure	<b>MAXALT</b>	
<i>Mevacor</i> * (lovastatin)	Elevated cholesterol	<i>Maxalt</i> (rizatriptan)	Migraine
<i>Moduretic</i> * (amiloride HCl-hydrochlorothiazide)**	High blood pressure	<b>CHIBROXIN</b>	
<i>Prinivil</i> * (lisinopril)**	High blood pressure and heart failure	<i>Chibroxin</i> * (norfloxacin)	Conjunctivitis
<i>Prinzide</i> * (lisinopril and hydrochlorothiazide)**	High blood pressure	<i>Cosopt</i> (dorzolamide hydrochloride timolol maleate)	Glaucoma
<i>Vaseretic</i> * (enalapril maleate and hydrochlorothiazide)	High blood pressure	<i>Timoptic</i> * (timolol maleate)	Glaucoma
<i>Vasotec</i> * (enalapril maleate)	High blood pressure and heart failure	<i>Timoptic-XE</i> * (timolol maleate)	Glaucoma
<i>Zocor</i> * (simvastatin)	Elevated cholesterol	<i>Trusopt</i> * (dorzolamide hydrochloride)	Glaucoma
<b>FOSAMAX</b>		<b>SINGULAIR</b>	
<i>Fosamax</i> * (alendronate sodium)	Treatment of post-menopausal osteoporosis	<i>Singulair</i> * (montelukast sodium)	Asthma
<i>Fosamax</i> * (alendronate sodium)	Prevention of post-menopausal osteoporosis	<b>COMIVAX</b>	
MK-677	Growth hormone deficiency	<i>Comivax</i> (haemophilus b conjugate [meningococcal protein conjugate] and hepatitis B [recombinant] vaccine)	Haemophilus influenzae type b and hepatitis B
<i>Propecia</i> (finasteride)	Male pattern hair loss	<i>M-M-R</i> * II (measles, mumps and rubella virus vaccine live)	Measles, mumps and rubella
<i>Proscar</i> * (finasteride)	Symptomatic benign prostate enlargement	<i>PedvaxHIB</i> * (Haemophilus influenzae type b conjugate vaccine)	Haemophilus influenzae type b
<b>PEPCID</b>		<i>Pneumovax</i> * 23 (pneumococcal vaccine polyvalent)	Adult pneumonia
<i>Pepcid</i> * (famotidine)	Ulcers and gastro-esophageal reflux disease	<i>Recombivax HB</i> * (hepatitis B vaccine [recombinant])	Hepatitis B
<b>CRIXIVAN</b>		<i>Vaqt</i> * (hepatitis A vaccine inactivated)	Hepatitis A
<i>Crixivan</i> * (lindinavir sulfate)	HIV infection	<i>Varivax</i> * (varicella virus vaccine live [Oka Merck])	Chickenpox
L-743,872	Antifungal	<b>ABAMECTIN</b>	
L-749,345	Antibiotic	<i>Abamectin</i>	Crop pests
<i>Mefloxin</i> * (sterile cefoxitin)	Antibiotic	<i>Enacard</i> * (enalapril maleate)	Canine heart failure
<i>Noroxin</i> * (norfloxacin)	Anti-infective	<i>Eprinomectin</i>	Cattle parasites
<i>Primaxin</i> * (imipenem-cilastatin sodium)	Antibiotic	<i>Ivermectin</i>	Animal parasites
		<i>Proclaim</i> * (emamectin benzoate)	Crop pests
		<i>Thiabendazole</i>	Crop fungal infestation
		■ Products in Development	
		■ Marketed Products	

\*This list excludes a number of older Company products.

\*\*Marketed in five European countries by The DuPont Merck Pharmaceutical Company.

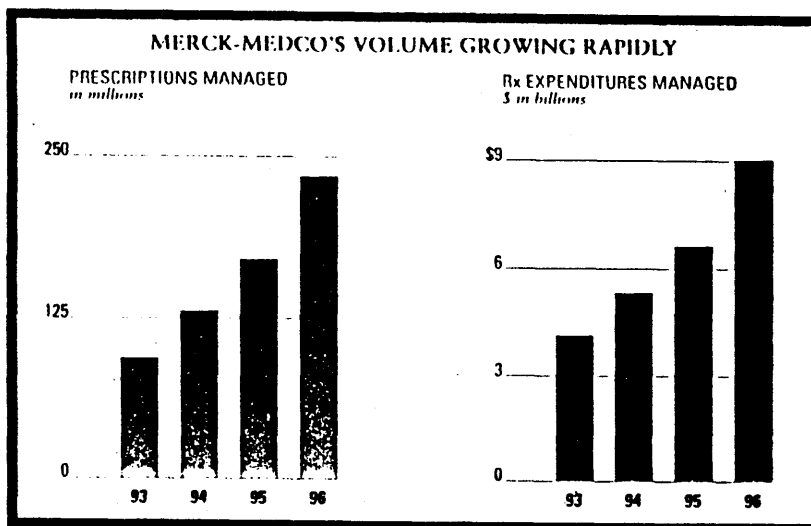
## Sales

(\$ in millions)	1996	1995	1994
Elevated cholesterol	\$ 4,055.9	\$ 3,211.1	\$ 2,599.0
Hypertension/heart failure	3,512.4	3,021.3	2,752.6
Anti-ulcerants	1,143.6	1,019.8	1,565.7
Antibiotics	822.3	848.3	827.4
Ophthalmology	693.1	570.6	482.3
Vaccines/biologicals	586.8	529.9	485.3
Benign prostatic hyperplasia	450.1	405.8	322.7
Osteoporosis	281.8	45.2	4.6
Other Merck human health	71.3	221.3	376.7
Other human health	7,167.3	5,726.7	4,103.9
Animal health/crop protection	1,044.1	1,041.9	1,027.4
Specialty chemical	—	39.2	422.2
	<b>\$19,828.7</b>	<b>\$16,681.1</b>	<b>\$14,969.8</b>

## Strategic Alliances

	1996	1995
Gastrointestinals		
Ethical	\$1,712.1	\$1,223.4
OTC	420.5	307.2
	<b>2,132.6</b>	<b>1,530.6</b>
Vaccines	663.0	598.6
Cardiovasculars	623.9	521.9
Radiopharmaceuticals	325.4	304.0
Central nervous system	267.7	247.5
Other	276.9	289.2
	<b>\$4,289.5</b>	<b>\$3,491.8</b>

## MEDCO SALES 1993-96 (Merck 1996)



## COSTS AND EXPENSES 1994-96 (Merck 1996)

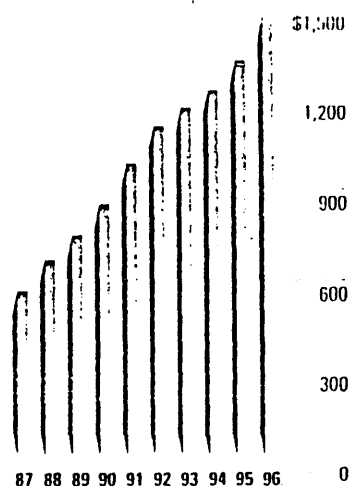
### Costs, Expenses and Other

(\$ in millions)	1996	Change	1995	Change	1994
Materials and production .....	\$ 9,319.2	+25%	\$ 7,456.3	+25%	\$ 5,962.7
Marketing and administrative .....	3,841.3	+16%	3,297.8	+ 4%	3,177.5
Research and development .....	1,487.3	+12%	1,331.4	+ 8%	1,230.6
Equity income from affiliates .....	(600.7)	+73%	(346.3)	*	(56.6)
Gains on sales of specialty chemical businesses .....	—	*	(682.9)	*	—
Gain on joint venture formation .....	—	*	—	*	(492.0)
Provision for joint venture obligation .....	—	*	—	*	499.6
Other (income) expense, net .....	240.8	-71%	827.6	*	232.8
	<b>\$14,287.9</b>	<b>+20%</b>	<b>\$11,883.9</b>	<b>+13%</b>	<b>\$10,554.6</b>

\* Over 100% or nonrecurring

## R&D EXPENDITURES 1987-96 (Merck 1996)

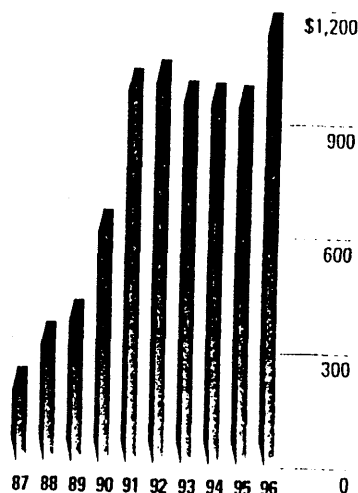
R&D EXPENDITURES  
\$ in millions



This chart excludes research and development costs incurred by the Company's joint ventures, which were \$440.7 million in 1996.

## CAPITAL EXPENDITURES 1987-96 (Merck 1996)

CAPITAL EXPENDITURES  
\$ in millions



*This chart excludes capital expenditures incurred by the Company's joint ventures, which were \$111.7 million in 1996.*

## CONSOLIDATED INCOME 1994-96 (Merck 1996)

Years Ended December 31  
(\$ in millions except per share amounts)

	1996	1995	1994
<b>Sales</b>	<b>\$19,828.7</b>	<b>\$16,681.1</b>	<b>\$14,969.8</b>
<b>Costs, Expenses and Other</b>			
Materials and production	9,319.2	7,456.3	5,962.7
Marketing and administrative	3,841.3	3,297.8	3,177.5
Research and development	1,487.3	1,331.4	1,230.6
Equity income from affiliates	(600.7)	(346.3)	(56.6)
Gains on sales of specialty chemical businesses	—	(682.9)	—
Gain on joint venture formation	—	—	(492.0)
Provision for joint venture obligation	—	—	499.6
Other (income) expense, net	240.8	827.6	232.8
	<b>14,287.9</b>	<b>11,883.9</b>	<b>10,554.6</b>
<b>Income Before Taxes</b>	<b>5,540.8</b>	<b>4,797.2</b>	<b>4,415.2</b>
<b>Taxes on Income</b>	<b>1,659.5</b>	<b>1,462.0</b>	<b>1,418.2</b>
<b>Net Income</b>	<b>\$ 3,881.3</b>	<b>\$ 3,335.2</b>	<b>\$ 2,997.0</b>
<b>Earnings Per Common Share</b>	<b>\$3.20</b>	<b>\$2.70</b>	<b>\$2.38</b>

## **BALANCE SHEET 1995-96 (Merck 1996)**

December 31  
(\$ in millions)

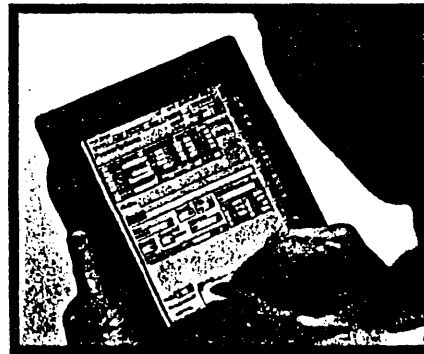
	1996	1995
<b>Assets</b>		
<b>Current Assets</b>		
Cash and cash equivalents	\$ 1,352.4	\$ 1,847.4
Short-term investments	829.2	1,502.4
Accounts receivable	2,655.9	2,495.7
Inventories	2,148.8	1,872.5
Prepaid expenses and taxes	740.3	899.5
Total current assets	7,726.6	8,617.5
<b>Investments</b>	2,499.4	1,969.6
<b>Property, Plant and Equipment (at cost)</b>		
Land	206.9	206.3
Buildings	2,949.8	2,783.2
Machinery, equipment and office furnishings	4,765.0	4,055.9
Construction in progress	804.7	663.6
	8,726.4	7,709.0
Less allowance for depreciation	2,799.7	2,439.9
	5,926.7	5,269.1
<b>Goodwill and Other Intangibles</b> (net of accumulated amortization of \$606.5 million in 1996 and \$411.5 million in 1995)	6,736.6	6,826.3
<b>Other Assets</b>	1,403.8	1,149.3
	<b>\$24,293.1</b>	<b>\$23,831.8</b>
<b>Liabilities and Stockholders' Equity</b>		
<b>Current Liabilities</b>		
Accounts payable and accrued liabilities	\$ 2,937.8	\$ 3,105.2
Loans payable and current portion of long-term debt	606.1	423.1
Income taxes payable	802.6	800.8
Dividends payable	482.7	418.2
Total current liabilities	4,829.2	4,747.3
<b>Long-Term Debt</b>	1,155.9	1,372.8
<b>Deferred Income Taxes and Noncurrent Liabilities</b>	4,027.3	3,689.7
<b>Minority Interests</b>	2,310.2	2,286.3
<b>Stockholders' Equity</b>		
Common stock		
Authorized - 2,700,000,000 shares		
Issued - 1,483,619,311 shares - 1996		
- 1,483,463,327 shares - 1995	4,967.5	4,742.5
Retained earnings	14,817.7	12,740.6
	19,785.2	17,483.1
Less treasury stock, at cost		
277,016,963 shares - 1996		
254,614,794 shares - 1995	7,814.7	5,747.4
Total stockholders' equity	11,970.5	11,735.7
	<b>\$24,293.1</b>	<b>\$23,831.8</b>

## ***Strong Investments in Information Technology***

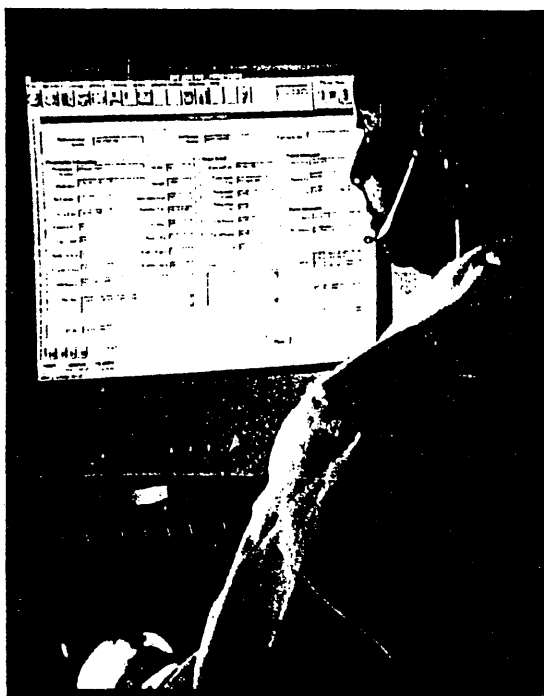
Achieving the full potential of managed pharmaceutical care is one of Merck's top strategic priorities. One way we are pursuing this priority is by investing strongly in information technology in order to enhance Merck-Medco's already strong capabilities in improving and managing the use of prescription drugs.

Information technology, for example, provides pharmacists and physicians with accurate data essential to our health management programs. Technology is essential, too, in serving patients and in handling more than 17 million incoming calls annually which Merck-Medco receives from patients. And technology is essential to support the continuing growth and increasing volume of our business.

The investments in technology – and new service initiatives being implemented across Merck-Medco – are further enhancing our ability to fulfill Merck-Medco's vision of being the most influential force in controlling health care costs and supporting improved patient care through the appropriate use of pharmaceuticals, benefiting payors and patients.

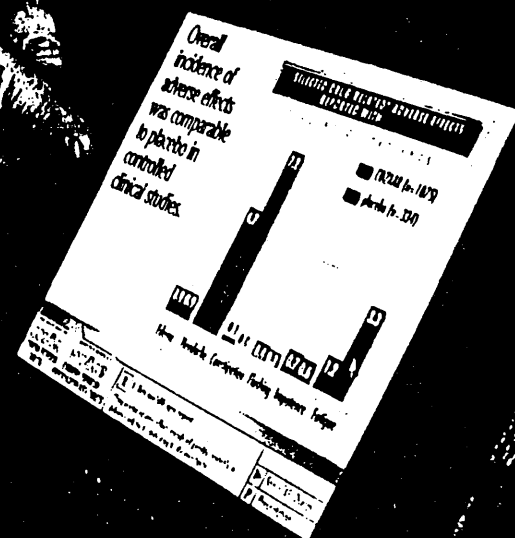


**The Vectis point-of-care program provides physicians with hand-held computers to access a patient's drug profile and the Merck-Medco formulary in the physician's office.**



**Customer Service Representative Avelyn Jackson fields a call, quickly accesses the patient's prescription information and reminds the patient that there is a refill due.**

Merck Executive Professional Representative Robert Comfort (r.) discusses results of clinical studies on the tolerability of our high blood pressure drug *Cozaar* with Gerald Miller, M.D., of Pennsylvania.



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